THE JOURNAL

OF THE

American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 165, NO. 1 — CHICAGO, ILLINOIS — SEPTEMBER 7, 1957

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THE PROBLEM OF FEVER IN PATIENTS WITH VALVULAR HEART DISEASE

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The clinical situation in which fever and valvular heart disease coexist presents a problem in differential diagnosis and management which is quite different from that associated with either condition alone. The causes of fever more or less peculiar to valvular heart disease are active rheumatic fever, bacterial endocarditis, drug fever, embolism, congestive heart failure, hemoglobin pneumonia, systemic lupus erythematosus, and atrial myxoma or thrombus. Bacterial endocarditis should be given first consideration when fever and heart murmur coexist.

THE proper interpretation of fever in patients with valvular heart disease can be one of the most perplexing problems confronting the internist. The clinical situation in which fever and valvular heart disease coexist presents a problem in differential diagnosis and management which is quite different from that associated with either condition alone. In a patient with fever and valvular heart disease, the physician must, of course, consider all the usual causes of fever. Individuals with heart murmurs have at least the usual susceptibility to the infectious, neoplastic, and other diseases which produce fever. It is with the group of diseases which causes fever more or less peculiar to valvular heart disease that we are primarily concerned.

We have been impressed with the relatively high frequency with which this problem arises in general hospital practice. No attempt has been made to review all the patients presenting this problem in the Johns Hopkins Hospital. Therefore, no statistical analysis of the final diagnoses or of the incidence of the condition is justified. However, 25 patients who posed this problem in striking form were observed by us during the years 1951 to 1954 when we were resident physicians of the Osler Medical Service. The conclusions reached are based on a review of these 25 cases listed in the table. The cases of three patients are described in detail in this paper (cases 1, 2, and 14).

The causes of fever more or less peculiar to valvular heart disease are as follows: 1. Active rheumatic fever (cases 1 through 10). 2. Postcommissurotomy syndrome (cases 11 and 12). 3. Bacterial endocarditis (cases 13 and 14). 4. Drug fever. 5. Embolism (cases 15 through 19). 6. Miscellaneous. Under this grouping are included congestive heart failure, hemoglobin pneumonia (cases 20 and 21), systemic lupus erythematosus (case 22), and atrial myxoma or thrombus (cases 23 through 25).

We have not attempted to give a comprehensive discussion of each disease. The discussion is oriented about the problem of the patient with fever and a heart murmur, and the various diseases are mentioned only as they enter into the consideration of such a patient.

Active Rheumatic Fever or Subacute Bacterial Endocarditis

In both cases 1 and 2 the major diagnostic possibilities were active rheumatic fever and bacterial endocarditis.

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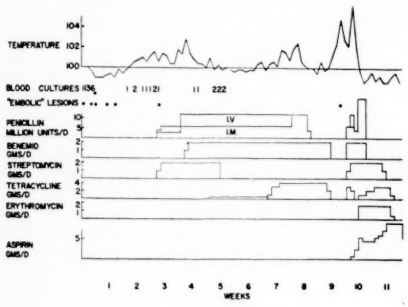
CASE 1.—A 27-year-old male schoolteacher gave no definite history of acute rheumatic fever, but exertional dyspnea and a heart murmur had been present since he was 12 years of age. The patient reported several illnesses characterized by episodes of fever and dyspnea, described as "pneumonia." Four months prior to the final hospital admission he complained of increasing exertional dyspnea, cough, orthopnea, and paroxysmal nocturnal dyspnea. There were several episodes of malaise, drenching night sweats, and temperature to 103 F (39.44 C); each of these episodes subsided with penicillin therapy. Three weeks prior to admission, painful swelling of the upper part of the abdomen was noted. For the first time the patient complained of swelling and stiffness of the ankles, knees, and knuckles. The joint symptoms persisted only a few days, but malaise, fever, and symptoms of increasing cardiac decompensation continued.

The patient was pale and chronically ill. Two typical splinter hemorrhages were seen beneath the nails of the second and fourth fingers of the right hand. There were a few fresh petechiae on the right side of the soft palate. There was no evidence of joint disease. There was generalized lymph node enlargement. The heart was enlarged. There were signs of mitral stenosis and atrial fibrillation. The liver was large and tender, but the spleen was not felt.

The patient's hospital course is illustrated in the figure. During the first two weeks the peripheral leukocyte count remained below 10,000 per cubic millimeter; the sedimentation rate



Clinical course of patient in case 1.

(Wintrobe-Landsberg method) was 30-40 mm. per hour; the hematocrit reading was normal. The urine contained neither albumin nor red blood cells.

Vigorous therapy was directed at the failing heart with essentially no effect. The patient remained afebrile, but new "embolic" lesions continued to appear. The splinter hemorrhages seen on admission disappeared, and new ones developed. In the mucous membranes, petechiae appeared and disappeared. Bacterial endocarditis was suspected because of the history of fever and the petechial lesions. Twenty blood cultures were obtained during this period of observation, and Streptococcus faecalis grew from one. In view of the positive culture and the numerous lesions, interpreted as embolic, it was decided to treat the patient for bacterial endocarditis.

During the third week he was started on therapy with 6 million units of penicillin and 2 Gm. of streptomycin-dihydrostreptomycin a day. During the first week of antibiotic administration, he showed no improvement, his fever increased, and, because of this apparent lack of response, tetracycline was also given. After five weeks, the penicillin and streptomycin were withdrawn, but tetracycline therapy was continued. For five days the patient remained afebrile, but then the fever recurred, with the temperature reaching 105 F (40.56 C) eight days after withdrawal of the antibiotics. New petechiae appeared; the patient complained of dyspnea and cough; and the leukocyte count rose to 20,000 per cubic millimeter. The hematocrit reading at that time was 43%.

The physicians managing the case felt obligated to reinstitute antibiotic therapy, and this was done at the end of the 10th week, with 6 million units of penicillin, 2 Gm. of probenecid (Benemid), 2 Gm. of tetracycline, and 1.6 Gm. of erythromycin being given daily. Blood cultures taken during the febrile period between courses of therapy were sterile. The temperature continued to rise in spite of the antibiotics, reaching 106 F (41.11 C) at the end of the 10th week. Throughout the hospital course, heart failure was a major problem. The patient's chief and often only complaint was dyspnea. It had been difficult to control the ventricular rate with 0.2 mg. of digitoxin a day, and the pulse deficit increased with the rising temperature. The patient required oxygen almost constantly. At the beginning of the 11th hospital week, aspirin in a dosage of 5-6 Gm. a day was given. With this regimen the temperature remained normal more consistently than at any time in previous weeks. The ventricular rate fell to 70 per minute. The patient remained afebrile for the next 11 days but continued to complain of dyspnea. During the 12th hospital week he developed acute pulmonary edema and died.

At postmortem examination, lesions of acute and chronic rheumatic fever were seen in the myocardium, endocardium, valves, and pulmonary artery. There were small organized thrombi in the lungs and liver. There was absolutely no evidence of active or healed bacterial endocarditis.

CASE 2.—At 13 years of age the patient in case 2 experienced an initial episode of painful swelling of the knees and ankles. She was first admitted to the hospital when she was 17 years old because of fever and increasing dyspnea after dental extractions. Physical examination revealed fever, the auscultatory signs of mitral stenosis, atrial fibrillation, and pulmonary congestion. The peripheral leukocyte count was 18,000 per cubic millimeter, and the sedimentation rate was 38 mm. per hour. The patient was treated with 2.4 Gm. of aspirin a day; with this treatment she became afebrile and improved symptomatically. She was discharged on maintenance therapy with aspirin and prophylactic sulfadiazine.

Nine weeks after discharge she was readmitted with fever, joint pains, and a rash. The fever and joint pains responded promptly to aspirin and bed rest. However, after two weeks of improvement the temperature rose to 101-102 F (38.33-38.89 C) and could not be controlled with aspirin in doses of 4.8 Gm. daily. The appearance of cutaneous petechiae aroused suspicion of bacterial endocarditis. Thrombosis of the right innominate vein developed, and because of this complication heparin sodium therapy was instituted. With great suddenness petechiae appeared on the soft palate, arms, and chest. The prothrombin time was found to be 50 seconds (prothrombin concentration was less than 25% of normal) on the day the petechial lesions appeared. No bishydroxycoumarin (Dicumarol) had been given, but it was felt that the combination of hepatic congestion and aspirin could well account for the prolonged prothrombin time. Vitamin K was given, with prompt return of the prothrombin time to 29 seconds (prothrombin concentration was 40% of normal). Petechiae continued to appear on the palate and the extremities. Repeated blood cultures were sterile. The temperature remained between 101 and 103 F (38.33 and 39.44 C). There was great difficulty controlling the heart rate with digitalis, and signs of cardiac failure increased. Because of the continuing fever, petechiae, and venous thrombosis, it was decided to treat the patient for bacterial endocarditis. Fifteen million units of penicillin was administered daily for three weeks, with a slow but definite response in the amount of fever. The response was of short duration.

During treatment with penicillin the patient developed tenderness at injection sites, and it was felt that chemical myositis might be contributing to her fever. After a week's observation of the patient while she was on therapy with penicillin, it was clear that her condition was worsening and the drug was withdrawn. The temperature dropped to normal as the myositis sub-

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sided. The patient developed massive swelling of the face and neck, presumably secondary to thrombosis of the major venous channels. Fever returned, and the patient died during the eighth week of hospitalization.

Rheumatic myocarditis with Aschoff bodies was found at autopsy. There was rheumatic endocarditis but no evidence of bacterial vegetations. There were thrombi in the atria; and multiple, remote and recent, pulmonary emboli were noted. There were multiple venous thromboses involving jugular and axillary veins.

endocarditis should be a prime consideration in a patient with rheumatic heart disease and fever. It is usually curable with proper treatment and is almost invariably fatal if treatment is withheld.

The diagnosis of endocarditis is confirmed by the demonstration of bacteremia; therefore, adequate blood cultures must be obtained as the first step in the investigation of fever in patients with valvular

Review of Twenty-five Cases of Valvular Heart Disease with Fever

Case No.	Sex	Age, Yr.	Heart Disease	Temperature, F (C)	Complicating Features	Cause of Fever	Remarks
1	M	27	Rheumatic heart disease, mitral stenosis, atrial fibrillation	101-103 (38.33-39.44)	Petechiae, splinter hemorrhages	Active rheumatic myocarditis (autopsy)	See text
2	F	17	Rheumatic heart disease, mitral stenosis, atrial fibrillation	101-103 (38.33-39.44)	Petechiae, venous thromboses, penicillin myositis	Active rheumatic myocarditis (autopsy)	See text
3	F	30	Rheumatic heart disease, mitral regurgitation	100-101 (37.78-38.33)		Active rheumatic fever (course)	Defervescence with hydroxy phenyl cinchoninic acid
4	F	36	Rheumatic heart disease, mitral stenosis	Low-grade, intermittent	Hematuria, pulmonary infarction, splinter hemorrhages	Active rheumatic endocarditis with multiple emboli (course)	All studies for bacterial endocarditis negative
5	F	35	Rheumatic heart disease, mitral regurgitation, aortic regurgitation	100-101 (37.78-38.33)	Intractable heart failure	Acute and chronic rheumatic myocarditis (autopsy)	
6	F	27	Rheumatic heart disease, mitral stenosis, aortic regurgitation, atrial fibrillation	100-101 (37.78-38.33)	Anemia, Roth's spots in fundus, night sweats	Rheumatic myocarditis (autopsy)	Dental extraction preceding admission
7	M	45	Rheumatic heart disease, mitral stenosis, mitral regurgitation, aortic regurgitation	101-102 (38.33-38.89)	Hematuria, myalgia, splenomegaly	Active rheumatic fever (course)	
8	F	30	Rheumatic heart disease, mitral stenosis	103 (39.44)	Heart failure	Active rheumatic myocarditis (course)	Activation of rheumatic fever after cardiac catheterization
9	M	19	Rheumatic heart disease, mitral stenosis, mitral regurgitation, aortic regurgitation	100-101 (37.78-38.33)	Heart failure, splenomegaly, digital clubbing, hematuria	Active rheumatic myocarditis (autopsy)	Perionyehial erythema also striking
10	F	36	Rheumatic heart disease, mitral stenosis	100-101 (37.78-38.33)	Heart failure, splinter hemorrhages	Re-stenosis of mitral valve after commissurotomy (autopsy)	No definite histological evidence of rheumatic activity, but re-stenosis of valve 4 yr. after operation taken as evidence of rheumatic activity. One blood culture positive for Streptococcus faecalis
11	M	24	Rheumatic heart disease, mitral stenosis	101-104 (38.33-40.00)	Petechiae; tender, swollen fingertips	Active rheumatic myocarditis (course)	"Postcommissurotomy syndrome"
12	F	36	Rheumatic heart disease, mitral stenosis	101-103 (38.33-39.44)	Pleural effusion, heart failure	Active rheumatic myocarditis (course)	"Postcommissurotomy syndrome"; no Aschoff's bodies in left atrium
13	M	34	Aortic regurgitation, rheumatic heart disease (?), syphilis (?)	100-103 (37.78-39.44)	Heart failure	Bacterial endocarditis (autopsy), syphilitic aortitis	20 blood cultures negative
14	M	18	Rheumatic heart disease, mitral regurgitation	98-102 (36.67-38.89)	Heart failure, pericarditis	Bacterial endocarditis, coronary embolism (autopsy)	Temperature fell with hydroxy phenyl cinchoninic acid, see text
15	F	39	Rheumatic heart disease, mitral stenosis, aortic regurgitation	100-103 (37.78-39.44)	Heart failure, splenomegaly, pulmonary infarction	Pulmonary and coronary embolism (autopsy)	Clinical impression: rheumatic myocarditis
16	F	41	Rheumatic heart disease, mitral stenosis, mitral regurgitation	100-102 (37.78-38.89)	Heart failure, atrial fibrillation	Subacute and chronic rheumatic endocarditis and myocarditis, splenic and cerebral embolism (autopsy)	
17	F	34	Rheumatic heart disease, mitral stenosis, aortic regurgitation	101-104 (38.33-40.00)	Pleural effusion, heart failure	Pulmonary and splenic embolism (autopsy)	
18	M	49	Rheumatic heart disease, aortic regurgitation, aortic stenosis	100-101 (37.78-38.33)	Petechiae, splinter hemorrhages, splenic infarction	Sterile embolization, 16 blood cultures negative (course)	Endocarditis treated 4 mo. previously
19	F	27	Rheumatic heart disease, mitral regurgitation	99-100 (37.22-37.78)	Splinter hemorrhages	Sterile embolization, 7 blood cultures negative (course)	Endocarditis treated 3 mo. previously
20	M	28	Rheumatic heart disease, mitral stenosis	99 (37.22)	Hemoptysis, night sweats	Chronic passive congestion of lungs, recent and organized pulmonary hemorrhage (autopsy)	Tuberculosis considered clinically
21	M	39	Rheumatic heart disease, mitral stenosis	103 (39.44)	Hemoptysis, night sweats	Hemoglobin pneumonitis (course)	381 million units penicillin for subacute bacterial endocarditis
22	M	44	Mitral stenosis	100-103 (37.78-39.44)	Hematuria, clubbed fingers, pericarditis, splenomegaly	Systemic lupus erythematosus (autopsy)	
23	F	58	Rheumatic heart disease, mitral stenosis, mitral regurgitation, (antemortem diagnosis)	100-102 (37.78-38.89)	Fever, weight loss, pulmonary and systemic embolism	Myxoma of left atrium, embolization of pulmonary and systemic circulations (autopsy)	
24	F	37	Rheumatic heart disease, mitral stenosis, mitral regurgitation	101 (38.33)	Syncopal attacks	"Ball-valve" thrombus, left atrium (autopsy)	
25	F	33	Rheumatic heart disease, mitral stenosis, mitral regurgitation, (antemortem diagnosis)	101-103 (38.33-39.44)	Systemic embolism	Myxoma, left atrium	Long treatment for subacute bacterial endocarditis

In both of these cases the incorrect diagnosis of bacterial endocarditis was made and treatment given. This diagnostic error cannot be criticized. Bacterial heart disease. There is a great deal of information in the literature concerning the number of cultures that may be considered adequate, the duration of the

culturing period, and ideal bacteriological techniques.[1] These factors should be considered before it is stated that bacteremia is not present.

In evaluating the results of the blood cultures it is important to remember the following points: (1) a certain percentage of patients with bacterial endocarditis (estimated at between 10-15%) have consistently negative blood cultures, as in case 13 [2]; (2) positive blood cultures may occasionally be obtained from normal individuals [1a] and from individuals with valvular heart disease who do not have endocarditis,[3] as in cases 1 and 10; and (3) when endocarditis exists, the blood cultures are usually either all positive or all negative.[1a] These considerations, for example, cast some doubt on the significance of the single positive culture in case 1 when 28 other cultures were negative.

The patients in both cases 1 and 2 died of the consequences of active rheumatic carditis. In case 1 the clinical diagnosis was not made until the last weeks of the patient's life. In both cases the attending physicians were led to the diagnosis of bacterial endocarditis by a variety of incorrectly interpreted findings.

The diagnosis of rheumatic activity in patients with long-standing rheumatic valvular disease is difficult. The classic manifestations of the disease as it is seen in children are often absent in adult patients, especially in those in the southern part of the United States.[4] The diagnosis of rheumatic activity is made especially difficult by the lack of a precise definition and even a single pathognomonic clinical criterion. Histological evidence obtained from atrial appendages removed at the time of mitral valve commissurotomy correlates poorly with clinical and laboratory findings.[5] The various serologic tests, usually positive in rheumatic fever, are of some use in following the course of the disease but are not specific, can be positive in other diseases, and, in general, are of limited diagnostic significance.[6]

The diagnosis of rheumatic fever is essentially a clinical one. Joint manifestations, erythema marginatum, and subcutaneous nodules are extremely helpful when present, but, in our experience, such definite signs are usually lacking in the type of patient under discussion. Minor arthralgias are common but often are no more prominent than the skeletal symptoms of individuals acutely ill with bacterial endocarditis. Objective evidence of joint involvement should, however, be considered clinical evidence of the highest order for the existence of rheumatic disease. In patients with long-standing rheumatic heart disease, fever and progressive cardiac failure may be the only signs of active rheumatic myocarditis. In retrospect, it is easy to see that fever and heart failure were the predominant manifestations throughout the courses of the patients in cases 1 and 2. Atrial fibrillation, associated with unusual difficulty in controlling the ventricular rate with digitalis, suggests active myocarditis. In the past there was a clinical axiom that bacterial endocarditis did not develop in patients with atrial fibrillation. Although it is clear that this axiom is not invariable, bacterial valvulitis does occur less frequently in these patients and, in general, in the advanced stages of valvular heart disease.

A therapeutic trial of aspirin is a dubious method for diagnosis of active rheumatism. In case 1 such a trial seemed helpful in that a fall in temperature and pulse rate and improvement in the degree of cardiac compensation accompanied the second course of aspirin. In contrast, there was no fall in temperature in the patient in case 2 when she was given 4.8 Gm. of aspirin a day, a dose which produced symptoms of salicylate intoxication. This lack of response was taken as evidence against active rheumatic fever and led to the diagnosis of bacterial endocarditis.

Whenever possible, therapeutic trials of antibiotic therapy should be avoided, as they are rarely helpful and often confusing. Antibiotics are frequently given to patients with fever and valvular heart disease on the basis of a presumptive diagnosis of bacterial endocarditis. It is impossible not to attach at least some diagnostic significance to the response of fever to this therapy, but this can be hazardous whether the temperature rises, falls, or remains unchanged. Body temperature is usually selected as the sign to follow for response to therapy, because it can be measured easily, graphed, and treated quantitatively. It is not, however, the only sign of therapeutic success in the treatment of bacterial endocarditis. Weight gain without heart failure, increase in appetite, and a general sense of well-being, though more difficult to evaluate, are possibly more reliable indexes of progress.

In the patients in cases 1 and 2, minor falls in temperature which coincided with antibiotic administration were taken as evidence corroborating the diagnosis of bacterial endocarditis. In case 1, after penicillin in a dosage of 6 million units per day had been administered for several days with no sustained fall in temperature, it was assumed that the dosage was inadequate. The dosage was doubled, and the temperature fell to the normal range. This sequence of events was taken as further confirmation of the diagnosis of bacterial endocarditis. A similar, although less impressive, response was interpreted as evidence for endocarditis in case 2.

Occasionally it is necessary to institute treatment for bacterial endocarditis without bacteriological confirmation of the diagnosis. In evaluating response to therapy, the following possibilities must be kept in mind: subsidence of fever may indicate the existence of endocarditis, or it may be only a chance variation in the course of another disease. Continued fever may indicate that the dosage is inadequate, that the correct drug is not being used, that the diagnosis is incorrect, or that the patient has developed a febrile reaction to the therapeutic agent.

As yet, the experience with the combination of antibiotics and adrenal corticoids in patients with subacute bacterial endocarditis is too limited to justify any final conclusion about either benefits or risks. Our personal experience is limited to a single

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patient in whom the administration of cortisone for a penicillin reaction had no evident adverse effect on the course of the subacute bacterial endocarditis treated concurrently with large doses of penicillin. In the literature good results are reported by some [7] and poor results by others.[8]

Drug Fever

Febrile reactions to antibiotics are largely responsible for the confusion associated with therapeutic trials. Penicillin, the most commonly used agent in the treatment of bacterial endocarditis, is capable of producing fever in at least two ways. When the fever rises gradually after a period of a week or more of intramuscular administration of penicillin, sterile inflammation at the injection sites should be suspected. In case 2, tenderness at the injection sites facilitated the diagnosis of chemical myositis. Often the patient does not complain, and it is only by careful palpation that the indurated, slightly tender areas of myositis are detected deep in the muscle. The diagnosis is confirmed by the gradual defervescence which accompanies the substitution of the intravenous for the intramuscular route of administration.

Fever caused by penicillin does not present a diagnostic problem when accompanied by a rash, but fever is often the only manifestation of hypersensitivity to the drug and prompt defervescence may follow its withdrawal. The serum sickness type of reaction [9] characterized by myalgia, arthritis, lymphadenopathy, and splenomegaly often closely simulates rheumatic fever and, therefore, assumes special significance in patients in whom rheumatic activity is always a definite possibility.

Fever may result from the use of many other drugs commonly employed in the management of patients with valvular heart disease. Febrile reactions to quinidine, procaine amide, and mercurial diuretics have been reported. In one of our patients, quinidine was responsible for fever, petechial hemorrhages, and splenomegaly—a clinical picture closely simulating bacterial endocarditis. To our knowledge, digitalis has never been proved to be responsible for drug fever, although urticaria has been observed [10] and we have recently seen erythema multiforme in a patient who received separate administrations of digitalis leaf and digitoxin.

Evaluation of Embolic Lesions

Petechial hemorrhages, embolism in retinal vessels, and "splinter hemorrhages" under the nails are important signs in patients with valvular heart disease. These lesions, commonly referred to as hemorrhagic or embolic, are usually thought to be pathognomonic of bacterial endocarditis, and often a prolonged course of penicillin therapy has been started because of one splinter hemorrhage or one shower of petechiae. These lesions are of great significance and should be diligently sought, but caution must be exercised in their interpretation.

Hemorrhagic and embolic lesions appeared periodically in patients in cases 1 and 2, and yet neither patient had bacterial endocarditis. These lesions have been noted in other patients with active rheumatic fever and in patients with the postcommissurotomy syndrome (case 11). A strikingly similar case has been reported in which splenomegaly, hematuria, and petechiae were seen in a patient dying of rheumatic carditis.[11] Petechial lesions and splinter hemorrhages may occur on the basis of the rheumatic process alone and in the absence of bacterial vegetations of the heart valves. The lesions may be the result of sterile embolization from fibrillating atria or rheumatic valvulitis or may represent a local vascular component of the rheumatic process. In two patients (cases 18 and 19) with long-healed bacterial endocarditis, splinter hemorrhages have been seen with no evidence of active infection, and it is presumed that sterile emboli from healed vegetations were responsible. Sterile emboli were apparently responsible for typical Roth's spots in the retinas in another patient (case 6) who did not have bacterial endocarditis.

Petechiae or splinter hemorrhages may occur from trauma, for example, in the oral cavity from ill-fitting dentures or in the nail beds from injury. Reactions to drugs, with or without thrombocytopenia, may be accompanied by hemorrhagic lesions, which, when few in number, may suggest bacterial endocarditis. Before petechial lesions are attributed to embolism it should be demonstrated that the blood coagulation mechanism is functioning normally. The hepatic congestion of heart failure can be accompanied by a prolonged prothrombin time and excessive bleeding. In case 2 the prolonged prothrombin time was attributed to the "bishydroxycoumarin-like" effect of aspirin superimposed on the impaired hepatic function resulting from congestion. This increased sensitivity of the congested liver to bishydroxycoumarin and aspirin is especially important, as both of these drugs may be given in the situation under consideration. Frick [12] attributes the bleeding tendency to a direct effect of salicylates on capillaries. The thrombosis of the great veins which occurred in case 2, while an unusual complication, occasionally develops with severe heart failure.

In both cases 1 and 2, old and recent pulmonary emboli were present. This finding is very common in patients dying with chronic rheumatic heart disease, particularly when atrial fibrillation has existed for an appreciable period (cases 4, 15, and 17). Pulmonary embolism without accompanying rheumatic myocarditis was a "good diagnosis" in case 1. The history of recurrent bouts of pneumonia suggests previous episodes of embolism. If the emboli are small, the classic signs and symptoms, such as cough, hemoptysis, friction rub, and typical x-ray changes, may be absent. As the pulmonary vascular tree is progressively occluded by embolization, chronic right ventricular failure can develop and the slowly developing pulmonary vascular obstruction may have effects resembling those of rheumatic myocarditis. Fever, progressive and un-

controllable heart failure, and tachycardia are sometimes the only manifestations of recurrent pulmonary embolism.

In cases 1 and 2 petechiae and splinter hemorrhages were encountered in association with active rheumatic carditis. Splenomegaly, another finding often considered specific for bacterial endocarditis, also occurs in patients with rheumatic heart disease in the absence of bacterial endocarditis.[13] Congestive heart failure or splenic infarction explains some, but by no means all, of these instances of splenomegaly. In cases 7, 9, and 15, and in cases reported by others, active rheumatic fever seemed, even at autopsy, to be the sole basis for the splenic enlargement. The patient in case 9, a 19-year-old boy who died with active rheumatic carditis, also had marked digital clubbing, perionychial erythema, and hematuria—all features commonly associated with bacterial endocarditis.

In cases 1 and 2 presented above, rheumatic myocarditis simulated bacterial endocarditis. In the case (case 14) below, an unusual complication of bacterial endocarditis led to the mistaken diagnosis of rheumatic myocarditis.

CASE 14.—An 18-year-old boy had developed fever, malaise, and fatigue five months prior to admission. He was admitted to another hospital where two blood cultures were positive for nonhemolytic streptococci and 47 million units of penicillin were administered over a period of 78 days. After discharge, the patient did well until two weeks prior to readmission, when he developed fever and pain in the joints. He was readmitted to the same hospital and given a short course of penicillin and tetracycline and then transferred to the Johns Hopkins Hospital.

He was found to have mitral stenosis and regurgitation. He was afebrile on admission, the peripheral leukocyte count was 9,800 per cubic millimeter, and the erythrocyte sedimentation rate was 21 mm. per hour. A rare erythrocyte was seen in the urine, but there was no albuminuria. Eleven blood cultures were sterile. On the seventh hospital day the patient awoke with severe precordial pain, which persisted for three hours and was accompanied by a fall in blood pressure. On the following day the temperature rose to 102 F (38.89 C), the peripheral leukocyte count rose from 7,800 to 27,000 per cubic millimeter, and a pericardial friction rub appeared. Electrocardiograms showed no significant change from that on the admission record. It was felt that this sequence of events was best explained by either a coronary embolus or acute rheumatic myocarditis and pericarditis. Treatment with hydroxy phenyl cinchoninic acid (an aspirin-like agent then under investigation) was instituted, resulting in the prompt fall of the temperature and leukocyte count to normal. The patient was discharged, essentially asymptomatic to convalesce at home. However, heart failure developed after discharge, and he returned after one month.

On readmission he was in severe heart failure. This was interpreted as a manifestation of progressive rheumatic myocarditis. He was afebrile on admission, but the temperature reached 101.4 F. (38.6 C) on the fifth hospital day and rose to approximately this level on each of the next three days. The peripheral leukocyte count was 12,000 per cubic millimeter, and the erythrocyte sedimentation rate was 7 mm. per hour. In one of the three urine specimens examined one red blood cell was seen, and in others a trace of albumin was noted. Three blood cultures were sterile. The patient died after one week in the hospital. At autopsy, vegetations containing microscopically demonstrable bacteria were found on the mitral valve. There were multiple subacute focal infarcts of the right and left ventricles and subacute rheumatoid endocarditis.

The combination of fever, leukocytosis, and pericardial friction rub in a patient with rheumatic heart disease most often indicates rheumatic pancarditis. In this case, however, while lesions of subacute rheumatic endocarditis were present at autopsy, the primary myocardial disease was infarction secondary to coronary embolism.

Miscellaneous Causes of Fever

In most patients with fever and valvular heart disease, rheumatic fever, bacterial endocarditis, drug fever, or embolism will be found to explain the fever. There are, however, several more unusual febrile disorders that deserve consideration in relation to these patients.

Congestive failure is included merely to state that per se it probably never produces sufficient fever to be important in the type of patient being discussed.[14] Oral temperatures of 99-100 F (37.22-37.78 C) may be attributed to congestive failure, but for fever of greater magnitude other explanation must be sought.

Systemic Lupus Erythematosus.—A 44-year-old man (case 22) was seen at autopsy to have had systemic lupus erythematosus manifested by mitral stenosis, fever, clubbed fingers, hematuria, splenomegaly, and petechial rash. The clinical diagnosis had been bacterial endocarditis, and, although blood cultures were negative, he received treatment for this infection. A circulating anticoagulant was present in this patient and contributed to petechial and other hemorrhagic manifestations. It is important to remember that lupus can produce valvular heart disease and that the manifestations of acute systemic lupus may simulate bacterial endocarditis and rheumatic fever.

Hemoglobin Pneumonia.—Hemoptysis is a familiar event in mitral stenosis. Rupture of bronchial varices is usually responsible; however, repeated massive hemoptyses associated with elevations of temperature may result from extensive rheumatic pneumonia and pulmonary vasculitis. Occasionally the aspiration of blood into the lung after a bronchial hemorrhage produces a clinical picture which may include fever as a leading feature. Shaking chills are not infrequent at the onset. Leukocytosis, elevation of the sedimentation rate, and mild bilirubinemia may be observed. Pronounced apprehension is rather characteristic and often develops without apparent reason before the other signs.[15] These attacks are usually nocturnal and often follow unusual exertion during the day.

Hemoglobin pneumonia is a satisfactory term for the generalized illness these patients may have. Patients often have physical and x-ray signs as a result of aspiration of blood into the lung, but these are not always present. Infiltrations concentrated at the base of the right upper lobe overlying the fissure are common, suggesting that the laws of "bronchial embolism" as defined by Brock apply here. Sometimes the pulmonary shadows fan out from each hilum in a "butterfly" pattern; this may be the result of a concomitant pulmonary edema.

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The mechanism of bilirubinemia is not clear, but it is probably similar to that responsible for icterus with pulmonary infarction. The pronounced systemic reactions—chills, fever, leukocytosis—may well be a response to altered blood in the airways. In many of these cases very little blood is necessary to evoke the reaction, thus suggesting that hypersensitivity plays a role. Pulmonary infarction obviously can produce much the same clinical picture and, of course, is frequent in patients with mitral stenosis. Usually, however, these two disorders can be distinguished from each other. Hemoglobin pneumonia represents a discreet entity worthy of consideration.

A striking case of hemoglobin pneumonia was that of the patient in case 21, a 39-year-old man with mitral stenosis who had been having intermittent attacks of shortness of breath and fever at night for two years prior to hospital admission. He had been studied at three different medical centers, and, because of fever, the diagnosis of endocarditis had been made despite the fact that all blood cultures were negative. He had received 381 million units of penicillin, but the attacks continued to occur while he was receiving antibiotic therapy. A typical nocturnal episode was characterized by apprehension, tachycardia, fever to 103 F (39.44 C), and leukocytosis of 23,500 cells per cubic millimeter. This was most likely to follow a day of unusual exertion. All the signs and symptoms subsided within 12 hours. The patient had a mitral valvulotomy for relief of pulmonary hypertension and when last heard from, one year after operation, reported amelioration of these symptoms.

Fever from Ball-Valve Tumors.—It is not generally appreciated that intracardiac tumors and thrombi may cause the presenting symptom of fever. One patient (case 24), when she was admitted to the hospital, had signs of rheumatic mitral stenosis and a low-grade fever. The major diagnostic possibilities were rheumatic fever and bacterial endocarditis, and both aspirin and penicillin were administered without effect. At autopsy, a pedunculated ball-valve thrombus was found in the left atrium and there was evidence of both recent and old pulmonary embolism. Fever and signs of peripheral embolism were prominent features in two other patients (cases 23 and 25) who proved to have myxoma of the left atrium with multiple tumor emboli. It seems probable that the fever in these patients arises in part from the process of embolization. The combination of fever, heart murmur, and peripheral embolism frequently leads to the mistaken diagnosis of bacterial endocarditis. At least one similar case of fever with auricular tumor has been described.[16]

Comment

Patients with valvular heart disease and fever present difficult problems in differential diagnosis and management. Bacterial endocarditis should properly be given first consideration when fever and a heart murmur coexist. Without deemphasizing the importance of bacterial endocarditis, one should also direct attention to other conditions which closely simulate it. Petechial lesions, splinter hemorrhages, clubbing of the fingers, and splenomegaly can appear during the course of active rheumatic fever. These lesions are not specific for bacterial endocarditis. Rheumatic myocarditis may be fatal if untreated. In cases in which the differentiation between rheumatic activity and bacterial endocarditis cannot be made with certainty and in which the patient is gravely ill, therapy probably should be directed at both diseases.

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HEMIPELVECTOMY FOR MALIGNANT DISEASE

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The results of amputating an entire lower extremity with the corresponding half of the pelvis for malignant disease in 50 patients seen before the end of December, 1954, are reviewed for the purpose of assessing the therapeutic value of the operation and identifying the factors that affect immediate surgical mortality. No hospital deaths occurred, but in 1955 a hospital death followed operation. It resulted from pulmonary embolism on the seventh postoperative day. This extremely low mortality is ascribed to the relatively short duration of the operative procedure (which averaged 2¼ hours), to the general supportive care given to the patient, and to the replacement of lost blood. A tracheal tube was used by the anesthesiologist in every case. The surgeon must avoid seeding the wound with tumor cells, and transabdominal biopsies of tumors of the os coxae during exploratory laparotomy or through the incision made at the time of hemipelvectomy are strongly condemned. The life expectancy of the patient depended on the type of diseases that necessitated operation, and the best postoperative survival rate was in the group of patients with chondrosarcoma.

Though the first successful transiliac amputation or hemipelvectomy was done by Girard [1] in 1895, it has been in only comparatively recent years that the making of a diagnosis of a malignant neoplasm of the bones or soft tissue of the pelvis and upper part of the thigh did not almost invariably amount to the signing of the patient's death warrant. The first resection was attempted in 1891 by Billroth.[2] His patient died in shock, as did several others on whom resection was attempted before Girard performed that first successful hemipelvectomy in 1895. As late as 1935, Gordon-Taylor and Wiles [3] were able to find in the literature only 79 reported instances of treatment by hemipelvectomy, with 46 operative deaths. The largest single group of cases to date is that reported by Gordon-Taylor and Munro [4] in 1952. They presented information on a total of 64 cases, with 14 deaths, or an operative mortality of 22%. It should be pointed out, however, that operations were performed in 11 of their cases prior to 1940 under conditions somewhat less favorable from the standpoint of supportive care than those enjoyed today. Four of these 11 patients died (36%), whereas 10 of 53 patients operated on after 1940 died, an operative mortality of only 19%.

The Series and Operative Mortality

The first hemipelvectomy at the Mayo Clinic was performed in 1943; in 1946, Beck, with one of us (W. H. B.),[5] reported 12 cases in which the operation was done at this clinic with no operative deaths. Through December, 1954, this series has been extended to 50 cases in which hemipelvectomy has been performed for malignant neoplasms of the pelvis and upper part of the thigh, still without an operative death. Hemipelvectomy was performed also during this time in two cases for intractable, advanced osteomyelitis of the innominate bone with multiple draining sinuses. Both of these patients recovered and are completely well. These two cases are not included in the 50 cases which form the basis of this report. Thirteen additional operations have been done but are not included in the series because of the brevity of follow-up. One of the patients operated on in 1955 died of pulmonary embolism on the seventh postoperative day. He had been ambulatory for several days prior to his death. This has been the only hospital death in the total of 65 cases in which hemipelvectomy has been done prior to Jan. 1, 1956, at the Mayo Clinic.

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Explanation for this extremely low mortality lies in several factors. Foremost of these is the excellent supportive therapy tendered by the members of the section of anesthesiology. Careful attention must be given to replacement of the blood lost, and even mild shock cannot be tolerated, since in a procedure of the magnitude of hemipelvectomy it may rapidly become irreversible. A total of 120,500 cc. (about 30 gal.) of blood was given to the 50 patients either during or immediately after operation, a rough average of 2,410 cc. (5 pt.) each. The most blood given to any one patient was 7,000 cc. and the least 1,000 cc. Levarterenol or ephedrine was given if necessary. A tracheal tube was used for all these patients so that respiration could be under the direct control of the anesthesiologist at all times.

Another important factor in maintaining low operative mortality is the duration of the operative procedure itself. The average operating time in all 50 cases was 2¼ hours, with the longest being 3½ and the shortest 1⅓ hours. In 13 of these cases the operat-

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ing time was less than two hours, and in only 7 was it more than three hours. It is obvious that the alarm reaction and stress mechanism of the patient are much more severely taxed by extremely long procedures, even with excellent supportive care; it must be remembered too that a difference of even one or two hours makes considerable difference (1) in the total amount of anesthetic agent given, (2) usually in the total quantity of blood lost, and (3) most certainly in the likelihood of postoperative complications.

Operative Technique

The operative technique described by King and Steelquist[6] was followed in most cases, although alterations were made as the occasion arose. In cases of tumors arising in the buttock, it was oftentimes necessary to form anterior instead of the standard posterior flaps in order to avoid the tumor. In a few of the cases in which tumors of the innominate bone protruded into the abdomen, a general surgeon assisted in the abdominal phase of the operation.

In all 50 cases, primary closure with rubber drains of the Penrose type was employed, with removal of the drains in 48 hours. Several of the stumps were slow in healing and drained for a week or two after operation, but in only three instances was healing a problem. In one case a large hematoma developed; it was evacuated repeatedly but re-formed. Finally, the margins of the flap were opened inferiorly, the defect was packed open, and the area was allowed to fill in by granulation. In the two other cases the margins of the flaps sloughed and skin grafting was necessary before final healing could be accomplished.

Injury to the genitourinary organs occurred in only one case, in which the urethra was lacerated when the pubic bone was removed. The defect in the urethra was immediately repaired by a urologic surgeon who was called in, and, except for the inconvenience of an indwelling catheter while healing took place, no difficulty was experienced and no sequelae were observed.

Perhaps the most important point in technique is emphasized by the fact that in 14 of the 25 patients who have died since operation, and in 2 of the patients who are now known to have metastases, seeding of the wound with tumor cells was known to have occurred at the time of operation. This resulted from (1) taking of a biopsy specimen through the future operative site before hemipelvectomy or through the operative site at time of hemipelvectomy; (2) the necessary removal of huge tumors in pieces which made it impossible to avoid some seeding with tumor cells, (3) adherence of the tumor to vessels, peritoneum, intra-abdominal organs, or tissue, such as parts of the sacrum that could not be removed, (4) incomplete removal of a tumor as a palliative procedure in cases in which it was obvious at the time of operation that complete removal was impossible, and (5) accidental opening of the tumor in the course of the operation.

No patient who now is living and without metastases is known to have had seeding of the wound with tumor cells; all patients in whom seeding is known to have occurred have either died or have definite evidence of recurrence. In one case, transabdominal biopsy of a chondrosarcoma of the ilium was carried out elsewhere, and, though the surgeon suspected that seeding had occurred at the time of the previous operation, this was not known for certain. This patient, contrary to the usual story, is living 12 months after operation and is without known metastases.

The removal of tissue from tumors of the innominate bone for microscopic examination and diagnosis at the time of exploratory laparotomy is to be deplored, as such practice often precludes any chance of complete eradication by hemipelvectomy later. The seriousness of the situation can usually be determined before operation and the patient's permission for radical operation obtained. Then, at operation, an approach suitable for biopsy can be employed. If the frozen section of the tissue removed reveals a malignancy, definitive treatment can be instituted immediately and the tissue near the incision used for the biopsy can be included in the portion removed. In this way, seeding the remaining tissues with tumor cells is avoided.

Duration of Symptoms and Survival

From a clinical standpoint, the 50 patients, for the most part, presented the symptoms and signs which would be expected from neoplasms of the pelvis for which hemipelvectomy was necessary. The usual symptoms were pain, mass, loss of motion in the hips, signs of nerve pressure and vascular pressure, and in some cases dysfunction of the bowel or bladder.

Of much more significance than the type of symptom presented, however, was the duration of the symptoms. Although some of these neoplasms are relatively slow growing and hence might show a good incidence of cure—even with symptoms of relatively long duration—for the most part, the shorter the time between onset of symptoms and removal of the tumor by hemipelvectomy, the better the chances of survival for the patient. Twelve of the 18 patients who had had symptoms less than six months at the time of operation are still living (two with metastases), and 4 of the 6 who had had symptoms for six months to one year are still living (one with metastases), while only 8 of the 25 patients who had had symptoms for more than one year have survived the present follow-up periods, and one of these has evidence of metastases.

A total of 25 of the original 50 patients who underwent hemipelvectomy are still living, though 4 of this group have generalized metastases. Discounting these four, the follow-up interval for these living patients ranges from the shortest period of five months to the longest of 11 years and eight months. In seven cases the follow-up period was five years or more; in

three it was between four and five years; in one, between three and four years, in two, between two and three years; in four, between one and two years; and in four, less than one year. The four patients with generalized metastases were living 22, 13, 6, and 2 months after operation when follow-up information was obtained.

Of the 25 patients who are dead, 13 did not survive the first year following hemipelvectomy, four lived one to two years, one lived about three years, five lived three to four years, and two lived six years and five years and five months, respectively, before dying of the neoplasm.

Selection of Patients for Operation

With adequate follow-up data now available on 50 patients, some conclusions may be drawn which may help to evaluate the efficacy of such a radical procedure as hemipelvectomy. Certainly the decision to recommend a hemipelvectomy must be the result of careful weighing of the many aspects by the surgeon who suggests such a course of action and by the patient before deciding to have it done. Aside from the immediate danger of loss of life during the procedure itself, a patient faces, on occasions, a rather stormy postoperative period and sometimes a prolonged convalescence, especially when any difficulty in wound healing is experienced.

TABLE 1.—*Survival After Hemipelvectomy, by Type of Lesion*

Lesions	Patients		
	Total	Living	Dead
Bone tumors			
Chondrosarcoma	22	13*	9
Osteogenic sarcoma	9	3	6
Fibroblastic	1	1	...
Osteoblastic	2	1	1
Chondroblastic	6	1	5
Reticulum-cell sarcoma	1	...	1
Total bone tumors	32	16	16
Soft-tissue tumors			
Fibrosarcoma	6	1	5
Liposarcoma	5	4†	1
Miscellaneous	7	4	3
Rhabdomyosarcoma	1	0	1
Myofibrosarcoma	2	2	...
Neurofibrosarcoma	2	1	1
Hemangiopericytoma	1	1*	...
Malignant mesenchymoma	1	...	1
Total soft-tissue tumors	18	9	9
Grand total	50	25	25

* 1 has metastases.
† 2 have metastases.

The disability associated with the loss of an entire lower extremity is not slight. The patient who has been engaged in active physical work is faced with the inability to return to this type of work, no matter how agile he may become on crutches or with use of a prosthetic appliance. Adjustments in his daily life must be made because the type of prosthesis available leaves much to be desired, particularly for older and heavier individuals. Driving a car presents problems in some instances. Bowel and bladder dysfunction, while not a prominent problem in our series, are certainly sequelae to be considered and can be disabling when they do occur. The third factor to be considered in elective hemipelvectomy is the tremendous psychic trauma associated with a mutilating procedure of this type. Many patients who can adjust to the idea of amputation of a leg are somehow unable to accept emotionally the loss of half of their pelvis as well, even though the resulting disability is almost the same.

It becomes obvious from the foregoing that careful consideration of each patient is imperative in selection of cases for hemipelvectomy. Not only must the surgeon assure himself to the best of his ability that distant metastases do not exist, but also he must weigh the operative mortality, stormy postoperative course, prolonged convalescence, resultant disability with the chance of sequelae, and psychic trauma against the possibility of obtaining a cure by this procedure. Since most patients will gladly accept the disadvantages for a reasonably good chance of permanent eradication of the tumor, consideration of the likelihood of cure in the different types of tumors is pertinent.

Survival as Related to the Type of Neoplasm

From a pathological standpoint, our patients were divided into two large groups, namely, those with primary tumors of bone and those with malignant neoplasms of soft-tissue origin. Tumors of 32 patients arose from bone. Of these 32 patients, 16 are living, although one has generalized metastases. These neoplasms of bone were of three general histological types: chondrosarcoma, osteogenic sarcoma, and reticulum-cell sarcoma (table 1).

The largest histological group of bone tumors was that of chondrosarcomas. Of the 22 patients in this group, 13 are living, including the one with generalized metastases previously mentioned. Follow-up periods in this group included the longest of 11 years and eight months without signs of recurrence, and the shortest of five months. Histologically, the chondrosarcomas were graded according to the classification of Broders, and the malignancy of all except one was found to be either grade 1 or 2 (table 2). Of the 10 patients with grade 1 malignancy, 5 are still living; of the 11 with grade 2 malignancy, 7 are living. The patient with the grade 3 chondrosarcoma is living three years and eight months after operation without signs of recurrence; and one of the patients with grade 2 chondrosarcoma has generalized metastases only six months after operation.

The location of the chondrosarcoma seemed particularly significant. The primary site of the chondrosarcoma was the femur in 7 of the 22 patients, and only 1 of these 7 has died. This patient, who was treated originally by disarticulation of the hip, had a recurrence in the stump involving the ilium. Hemipelvectomy was performed because of the recurrence one year later. Eight of the 15 patients with chondrosarcomas of the innominate bone have died.

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Of the nine patients who had osteogenic sarcoma, only three have survived (table 1). Histologically, all three types of osteogenic sarcoma were represented in the group: one tumor was of the fibroblastic type (grade 2); two were of the osteoblastic type (grade 3 and grade 4); and six were chondroblastic osteogenic sarcomas, two of which were of grade 2 and four of grade 3 malignancy (table 2). Two of the three living patients who had osteogenic sarcoma had neoplasms of grade 2 malignancy, while the third had a typical grade 4 osteoblastic osteogenic sarcoma involving the entire upper part of the femur complicated by a pathological fracture. This last patient had one of the longest follow-ups in the series (nine years and two months) and apparently can be considered well.

One primary tumor of bone was a reticulum-cell sarcoma which involved the upper part of the femur, the innominate bone, sciatic nerve, femoral vessels, and femoral nerve. There was massive brawny edema of the entire extremity, with exquisite intolerable pain resulting from involvement of the nerve. Hemipelvectomy was done as a palliative procedure to relieve the excruciating pain and remove the greatly enlarged useless extremity. Intensive x-ray therapy was given to this ordinarily radiosensitive tumor, but the patient lived only seven months. Death was due to generalized involvement.

The second large group of neoplasms, the soft-tissue tumors, consisted of two main and several miscellaneous types. There were six fibrosarcomas, five liposarcomas, and seven in the miscellaneous group. Of the 18 patients in this group, 9 were living at the time of follow-up, but 3 of these had evidence of generalized metastases (table 1). The longest follow-up period in this group was eight years and four months and was for one of the patients with myofibrosarcoma. The shortest follow-up period was seven months and two others were less than one year.

Only one of the six patients with fibrosarcoma is living. This patient, who had a grade 4 neoplasm, is living 18 months after operation and does not have any signs of recurrence. Of the five patients with liposarcoma, the one with the lesion of grade 1 and all three of the patients with lesions of grade 3 are living, although two of the latter have evidence of metastases. One of these patients with a grade 3 liposarcoma had a solitary metastatic lesion in the lung 16 months after hemipelvectomy. Pneumonectomy was performed on the right. The patient is living nine months after this second operation, and, while definite proof of other metastatic lesions cannot be demonstrated, it is suspected that such lesions exist.

The miscellaneous group of soft-tissue tumors is listed in table 1. Of the seven patients in this group, the two with myofibrosarcoma and one of the two with neurofibrosarcoma are living and are without evidence of metastases. The patient with a hemangiopericytoma has evidence of extensive pulmonary metastases 13 months after hemipelvectomy.

From the foregoing, several general impressions may be gained. By and large, the greatest percentage of survivals for the follow-up period was in the group of patients having chondrosarcomas. This might be expected, since chondrosarcomas are usually of a lower grade of malignancy, and more clearly differentiated grossly, which allows greater success in attempts at complete removal. Furthermore, many of the soft-tissue tumors occurred relatively high in the buttock or groin, making removal of all malignant cells less likely, particularly when these tumors are ordinarily poorly demarcated. The importance of location of the tumor, even among the chondrosarcomas, has already been pointed out. It is impossible to attach significance to survival associated with lesions of different grades of malignancy within groups (other than between groups having characteristically different grades as a group), since complete circumstances are not known in some cases and the groups are not large enough to present statistically valuable data. There are instances of relatively long follow-ups of patients with neoplasms of grade 4, whereas patients with neoplasms of grades 1 and 2 of the same histological type lived only a few months.

TABLE 2.—*Survival After Hemipelvectomy, by Grade of Malignancy of the Bone Tumors and Three Soft-Tissue Tumors*

Neoplasm	Grade	Patients	
		Living	Dead
Chondrosarcoma	1	5	5
(22 cases)	2	7*	4
	3	1	...
Total		13	9
Osteogenic sarcoma (9 cases)			
Fibroblastic	2	1	...
Osteoblastic	3	...	1
	4	1	...
Chondroblastic	2	1	1
	3		4
Total		3	6
Fibrosarcoma	2	...	1
(6 cases)	3	...	4
	4	1	...
Total		1	5
Liposarcoma	1	1	...
(5 cases)	3	3†	...
	4	...	1
Total		4	1
Neurofibrosarcoma	2	1	...
(2 cases)	4	...	1
Total		1	1

* 1 patient has metastases.
† 2 patients have metastases.

Postoperative Discomfort, Use of Prosthesis, Vesical and Bowel Dysfunction

From questioning the 25 survivors, it was learned that a relatively high percentage have experienced varying degrees of phantom pain. Although this phenomenon is an almost constant finding during the first few weeks after operation, the discomfort is usually of only short duration. Five of the patients stated that they had occasional mild pain that seemed to arise from the amputated extremity. These episodes had occurred periodically throughout the follow-up period.

Six others classified their discomfort as moderate and more or less constant. The pain was described as severe by four, being so severe in one as to require chordotomy for relief. In only these four cases has the pain been severe enough to be disabling per se. There were no symptoms of bowel or bladder dysfunction in any of the patients comprising this series with the exception of the case mentioned in which chordotomy was done because of persistent pain.

Only two of the patients stated that they routinely use a prosthesis, though two others mentioned that they had tried various prosthetic appliances and had found none satisfactory. The remainder of the survivors have not tried to use a prosthesis, either on advice of the limb maker or because of their own disinclination. Many of these patients have felt that they fared so well on crutches that they did not believe that any type of prosthetic appliance could offer additional comfort or function.

The local physician of one of the patients reported that the patient became pregnant some months after operation, enjoyed a relatively uneventful pregnancy, and spontaneously delivered a normal, healthy child. It is now three years and eight months since hemipelvectomy was done on this patient for grade 3 chondrosarcoma of the upper part of the femur.

Conclusions

On the basis of 50 cases in which malignant neoplasms of the pelvis and upper part of the thigh were treated by hemipelvectomy at the Mayo Clinic, the following points seem worth stressing:

1. The chances of survival are definitely improved by early recognition and operation soon after discovery of the tumor.

2. Chances for survival seem much greater in the slower-growing neoplasms, but anaplasia per se is not a contraindication, since some of the longest survivals in the series have been among patients with neoplasms of grades 3 and 4.

3. Location is an important factor in determining chances for survival, since tumors that can be removed *in toto* with a wide margin of normal tissue offer the best chance of complete eradication. This is best illustrated by the fact that the percentage of survivors among those who have had chondrosarcomas occurring in the upper part of the femur was much greater than among those who have had chondrosarcomas arising primarily from the innominate bones.

4. The highest percentage of survivals was in the group of patients with chondrosarcoma. This is thought to be due to the fact that as a group chondrosarcomas are usually of lower grade and are slower growing than other neoplasms removed. In addition, when they occur in the upper part of the femur, they often offer a wider margin of normal tissue and hence an excellent chance of cure in this location.

5. Transabdominal biopsy of tumors of the innominate bone at the time of exploratory laparotomy and biopsy of lesions through the same incision as that contemplated for hemipelvectomy are to be strongly condemned, since the chances for complete eradication are materially lessened because the procedures almost invariably allow seeding of the remaining tissue with tumor cells.

6. Operative mortality can be greatly lessened by careful supportive therapy, including meticulous replacement of blood, and by maintenance of a minimal operating time.

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The Return of the Patient.—Every doctor is interested in rehabilitation. That is what he means by the word "cure." By that term he means the relief of symptoms, the restoration of function and the return of the patient to his job, to his family, and to the community as a normal person. In the case of appendicitis, simple fracture or pneumonia, the doctor can achieve this end result with his own bare hands. When a person has lost a leg by amputation, suffered injury to the spinal cord, with paraplegia, or to the brain, with hemiplegia, however, the doctor needs not only his two hands but other hands as well. Unless the doctor's efforts are supplemented by the work of paramedical personnel, such a patient will be left permanently disabled, a burden to the family and community, and unable to assume his rightful place in society. . . . The philosopher Paulsen said that the object of all help is to make help superfluous. This is the ideal that has pointed the way to surgeons. It is an ideal that can be realized only when surgeons assume a fierce belief in their individual responsibility for what happens to their fellow men.—Henry H. Kessler, M.D., Rehabilitation of the Amputee, *Journal of the International College of Surgeons*, September, 1956.

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PREDNISONE AND PREDNISOLONE THERAPY IN RHEUMATOID ARTHRITIS

CLINICAL EVALUATION, WITH EMPHASIS ON GASTROINTESTINAL MANIFESTATIONS IN ONE HUNDRED FIFTY-SIX PATIENTS OBSERVED FOR PERIODS OF FOUR TO FOURTEEN MONTHS

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Rheumatoid arthritis was treated in 156 patients by oral administration of either prednisone or prednisolone. The initial dosage ranged from 10 to 40 mg. per day, given in divided doses at approximately six-hour intervals. In most patients, 10 mg. or less per day sufficed for maintenance. Therapy was continued for periods ranging from 4 to 14 months. Observations showed general improvement in the patients by subjective and objective criteria; functional capacity was increased, and 38 of the 59 adult male patients were enabled either to return to work or to continue their work status. Side-effects of these drugs were, in general, not disturbing, but the incidence of gastrointestinal complaints increased from 11 to 21%. Peptic ulcers appeared in some patients in whom the roentgenograms had not shown such lesions before treatment. Among five patients who developed complications of peptic ulcer, three developed hemorrhages and two suffered perforations. Because these complications offset somewhat the undeniable benefits of the prednisone and prednisolone to arthritic patients, there is urgent need for the development of drugs that will be equally effective and less marred by side-effects.

Six years of experience with corticotropin (ACTH) and adrenal cortical steroids in the management of rheumatoid arthritis has reemphasized the importance of a basic therapeutic program, which includes adequate rest, physical therapy, salicylates, relief from various types of physical and emotional stress, analgesia and sedation.[1]

In a clinic to which persons with more advanced rheumatoid arthritis and those who are more seriously ill are referred, conservative management, even diligently applied, may not suffice. Sustained progression of the rheumatoid process, increasing incapacity of the individual, and pressing socioeconomic need for earliest functional rehabilitation may force the clinician to add an adrenal cortical steroid to the basic therapeutic regimen.

In our practice the steroids have not been used as substitutes for the basic program of management, but rather as a supplementary measure. Although our emphasis in this presentation is on the clinical evaluation of the steroid effect, the common denominator of therapy was, in all instances, a relatively uniform program of general measures.

Prednisone and prednisolone, employed in the management of rheumatoid arthritis for nearly two years, have demonstrated the value of their antiphlogistic effect in this disease.[2] By clinical appraisal, the antirheumatic potency of prednisone, per milligram, generally averages four times that of hydrocortisone.[3] With amelioration of the manifestations of the disease, there is often increased functional capacity of the individual. Undesirable physiological effects have, however, been noted with prednisone as with cortisone and hydrocortisone.[4]

We are, therefore, attempting an appraisal of the value of prednisone by evaluating our experience in 156 patients with rheumatoid arthritis in whom prednisone (or prednisolone) was employed in an office and hospital practice from December, 1954, to the time of writing. We hoped that our data might shed some light on the following questions: What is the indication for the use of this steroid? What is the optimal dosage? What positive therapeutic effects may be expected? What undesirable effects may be anticipated? What measures may be taken to prevent or manage the undesirable effects which develop? What conclusions are justified with regard to the place of these steroids in the management of rheumatoid arthritis?

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Composition of Clinical Material

Prednisone was administered chiefly to patients with far-advanced, severe, but potentially reversible rheumatoid arthritis. Others were patients with early, milder, but unequivocal rheumatoid arthritis, in whom functional rehabilitation, which was a pressing necessity, could not be achieved by a fair trial of conservative measures alone.

Sixty patients were male; 96 were female. The ages ranged from 9 to 79 years. The majority of the patients (71%), were between 40 and 60 years of age.

In 46% of the cases, the duration of the arthritis was from 3 to 15 years. Twenty-seven per cent of the patients had had their disease over 15 years.

Six per cent of the patients were in stage 1 of their disease, according to the Steinbrocker classification.[4] Twenty-four per cent were in stage 2, 52% in stage 3, and 18% in stage 4. Prior to the institution of prednisone therapy, 63% of the patients were taking either cortisone or hydrocortisone. Seventeen per cent were receiving salicylates, and 20% were receiving phenylbutazone (Butazolidin) or chrysotherapy, with unsatisfactory response.

DURING PREDNISONE THERAPY

BEFORE PREDNISONE THERAPY — GRADE	I	II	III	IV	TOTAL
I					
II	18	42	2		62
III	2	67	21		90
IV		1	1	2	4
TOTAL	20	110	24	2	

Fig. 1.—Activity of rheumatoid arthritis, graded from 1 to 4, in increasing order of severity. Unstippled area shows number of patients in whom improvement with prednisone was sufficient to justify a lower grading.

Mode of Administration

In the majority of the patients (94% of the group) the initial dosage ranged from 10 to 40 mg. of prednisone or prednisolone per day, given in divided doses at approximately six-hour intervals. In 49% of the group the dosage range was 10 to 20 mg. daily. In five cases, dosages of 60 to 90 mg. daily were administered for periods of less than a week. The dosage was then adjusted according to the particular requirements of the patient. For maintenance therapy, 10 mg. or less of the drug per day was used in the majority of patients. At the time of analysis of our results, the duration of therapy ranged from 4 to 14 months. Eighty-two per cent of the patients have been observed while on prednisone therapy for at least an 8-month period and 66% over a 10-month period.

Results of Therapy

The results of therapy were evaluated from three points of view. The first was grading of the over-all improvement in the total activity of the disease as judged by composite evaluations of improvement in subjective and objective manifestations, general constitutional reaction, and the usual routine laboratory data. The next was the improvement in functional capacity of the individual. The third was the ability of the 59 adult male patients to either return to work or continue their work status.

Figure 1 presents an evaluation of the activity of the disease, relating the patient's status prior to treatment with his status on prednisone therapy. The degree of severity is graded from 1 to 4, in increasing order of severity. Prior to therapy, no patient was considered to have disease of grade 1 severity. During therapy, 20 patients were so classified. Eighty-nine patients, (57% of the total group) improved at least one grade with prednisone therapy.

Figure 2 shows the functional classification before and during therapy, according to Steinbrocker and others,[5] with severity of impairment classed from 1 to 4. Before treatment with prednisone there were no patients in class 1; during therapy 26 patients moved into this classification. Prior to therapy, eight patients were considered to have class 4 impairment; that is, they were partially or totally dependent upon others for basic activities of daily living. With therapy, only three remained in this classification. Sixty-four patients (41%), represented in the unstippled area in figure 2, improved sufficiently with prednisone to justify a higher functional classification.

DURING PREDNISONE THERAPY

BEFORE PREDNISONE THERAPY — CLASS	I	II	III	IV	TOTAL
I					
II	21	57			78
III	5	33	32		70
IV			5	3	8
TOTAL	26	90	37	3	156

Fig. 2.—Effect of prednisone therapy on functional capacity (classification according to Steinbrocker and co-workers[5]). Unstippled area shows number of patients in whom improvement with prednisone was sufficient to justify a lower classification.

An analysis of the work status of the 59 adult male patients included in this study is represented in figure 3, which indicates that 9 of the 30 patients who were not working at the start of therapy returned to work

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some time during the course of treatment with prednisone The 29 patients who were working maintained this status, although several of these experienced short periods of unemployment resulting from temporary flares of rheumatoid activity.

Undesirable Effects of Therapy

Nearly all of our patients receiving prednisone exhibited some manifestations of adrenal cortical hyperfunction (Cushing's syndrome), such as moon facies, buffalo obesity, increased appetite, insomnia, striae, and ecchymoses. The severity of these signs was generally proportional to dosage of prednisone and/or duration of therapy. In general, these manifestations were tolerated by the patient as a nuisance of relative unimportance. Edema and elevation of blood pressure were notably rare. This was in contrast to our previous experience with equivalent doses of hydrocortisone, when water retention was evident in the majority of instances.

The most disturbing side-effects noted were those referable to the digestive tract. Dyspepsia, referring to indigestion, heartburn, epigastric distress, or sour eructations (symptoms simulating those of peptic ulcer), occurred in 25% of our patients before prednisone therapy. After the institution of therapy, 48% exhibited dyspepsia of some degree. Considering only those patients with moderate to severe dyspepsia, it was again demonstrated that under therapy a twofold increase developed in the number of patients with this degree of gastrointestinal difficulty (11% before; 21% during therapy).

X-rays of the upper gastrointestinal tract were obtained in 43 patients who exhibited severe or persistent dyspepsia during treatment. Findings in 32 of these were normal. In three cases a diagnosis of hypertrophic gastritis was made, but no evidence of ulceration was noted. In one patient a scarred duodenal cap, without an ulcer niche, was demonstrated.

In four patients, two of whom were male, duodenal ulcers were seen. In one of these an x-ray of the gastrointestinal tract made prior to therapy had been normal. All four developed disturbing dyspepsia after administration of the steroid, in a dosage ranging from 10 to 20 mg. per day, for a period of 4 to 10 months.

Three female patients were noted to have a gastric ulcer on gastrointestinal x-rays made three to four months after prednisone therapy was begun and while they were receiving a dosage ranging from 6 to 10 mg. per day. In one of the three an x-ray of the gastrointestinal tract made prior to therapy had been normal. All three had mild dyspepsia prior to therapy, and in two of the three the distress increased markedly with the addition of prednisone.

Five patients developed complications of peptic ulcer. Three of these, who were taking from 10 to 25 mg. of prednisone per day, developed hemorrhage; in the other two the ulcers perforated. One patient with a history of gastrointestinal bleeding four years previously while on phenylbutazone therapy, who failed to adhere to a prescribed ulcer regimen, developed gastric hemorrhage during the third month of prednisone therapy. The second patient, a woman with severe rheumatoid arthritis who was obese, hypertensive, and plethoric, and who had been on corticotropin or hydrocortisone medication for years, died from gastrointestinal hemorrhage during the seventh month of therapy. The third patient, who developed a bleeding ulcer during the second month of treatment, required a subtotal gastric resection. Two patients, receiving 10 and 15 mg. of prednisone per day, respectively, developed perforations of duodenal ulcers 3 months and 12 months after the institution of therapy. These were successfully repaired surgically. In one of these patients x-rays of the gastrointestinal tract made prior to therapy had been normal.

		WORKED DURING PREDNISONE THERAPY		
		NO	YES	TOTAL
WORKED BEFORE PREDNISONE	NO	21	9	30
	YES	0	29	29
	TOTAL	21	38	59

Fig. 3.—Gainful employment status of 59 male patients.

Despite evidences of peptic ulceration, in 11 of the 12 patients described above it became necessary to resume prednisone therapy. This was combined with a strict ulcer regimen and was well tolerated. In addition, there were two patients with a diagnosis of peptic ulcer made many years before in whom prednisone therapy was instituted, combined with an ulcer program. Two other patients, one of whom had been receiving cortisone, exhibited gastric ulcer on x-rays of the upper gastrointestinal tract made prior to the institution of prednisone therapy. Gastric resection was performed in one of these cases before institution of therapy.

Effect on Gastric Secretion

Impressed with the relatively high incidence of dyspepsia, we undertook a study in which gastric analyses (with use of Ewald's test meal), including pH and free and total acid measurements, were per-

formed on 6 rheumatoid arthritics before and after prednisone therapy and on 10 rheumatoid patients after institution of therapy with prednisone.

In five of the six cases studied, there was an increase in free and total acidity, with a drop in pH values. Although statistically significant, this increase was not to values as high as those usually observed in patients with ulcer. Moreover, even though prednisone increased gastric acidity in most cases, there was no consistent correlation between this increased acidity and the presence of peptic ulcer. The latter was associated in some instances with a normal range of free hydrochloric acid or with relatively slight increases. The experience of Kammerer and Rivelis [6] was quite similar to our own.

Effect on Glucose Tolerance

In three patients previously aglycosuric, marked glycosuria and hyperglycemia developed. Two of these patients require insulin at present. In six other patients in whom either decreased glucose tolerance or overt glycosuria and hyperglycemia were present prior to therapy, the administration of prednisone was followed by the appearance of glycosuria or an increase in the insulin requirement.

Two patients developed fractures while on prednisone therapy. In one patient a fractured femur appeared after severe trauma. In the other, a severe degree of osteoporosis, present for many years, possibly contributed to the fracture which developed after mild trauma. The latter patient had been receiving steroids for years prior to the institution of prednisone therapy and had had a prolonged period of immobilization in bed prior to ambulation with crutches.

Deaths

In the entire group of 156 patients, there were 3 deaths. One patient died of bile duct cancer, another of generalized vasculitis with involvement of the mesenteric vessels and perforation of the colon, and the third from a bleeding peptic ulcer.

Comment

Our present evaluation of the effect of prednisone in rheumatoid arthritis confirms our earlier impressions regarding its effectiveness in lessening the activity of this disease, thereby improving the functional capacity of the individual. If it is remembered that the majority of our patients had relatively far advanced, severe forms of the disease, and that most of them had been receiving hydrocortisone ineffectually prior to substitution of prednisone, then the restoration and maintenance of some degree of functional integrity of the individual for periods of 4 to 14 months represents an impressive accomplishment. Fifty-seven per cent of the patients had a measurable decrease in total severity of the disease. Forty-one per cent had measurable improvement in functional capacity, and 9 out of 30 male patients who were not working returned to work through the effect of prednisone.

With wider experience and with increasing effort to ward off undesirable effects of the steroid, we found it expedient to reduce the dosage of prednisone in the majority of patients to a maintenance level of 10 mg. per day or less. To be sure, the fullest degree of functional restoration was not achieved, but, with less exposure to hypercortisonism, the long-continued administration of the steroid demanded by the chronicity of this disease may be facilitated.

Minor side-effects noted in the majority of patients were not disturbing. Most patients with salt and water retention resulting from hydrocortisone lost the edema or the degree of fluid retention decreased markedly when prednisone was substituted, with actual improvement in functional capacity of the individual. The rare instances of fluid retention during prednisone therapy could be readily controlled by restriction of salt in the diet.[2b]

Gastrointestinal complications constituted the most disturbing undesirable effects of therapy. Since pretreatment gastrointestinal x-rays were not obtained routinely, we are unable to draw conclusions concerning the development of peptic ulcer with prednisone. Peptic ulcer was demonstrated, however, during treatment with prednisone in 7 of 43 patients in whom gastrointestinal x-rays were obtained because of the severity of symptoms. Gastric hemorrhage or perforation of an ulcer developed in five additional cases.

It is of practical interest that in all of our patients who developed dyspepsia while on prednisone therapy, and in the four patients with a history of previous ulcer, administration of an aluminum hydroxide gel preparation and a diet incorporated in an ulcer regimen, generally combined with some reduction in the dosage of prednisone, appeared to relieve digestive symptoms.

A similar program of dietary and antacid medication permitted the continuation of prednisone medication, which was indispensable in all four patients with duodenal ulcer, in the three female patients with gastric ulcer, in two of the three patients who had bleeding peptic ulcers and in the two patients who had perforation of their ulcers. Without the steroid three of these patients were bedridden and unable to care for any of their most basic needs. With reinstitution of prednisone therapy in a dosage of 15, 10, and 5 mg. daily, respectively, one patient became ambulatory, the other could get around with the aid of crutches, and the third maintains a wheelchair existence. In all such cases, the absolute necessity for reinstituting prednisone therapy seemed to justify the potential risk involved. On this regimen the patients were not only free of dyspepsia but the

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gastrointestinal x-rays became normal and have remained so. This suggests that, when it is absolutely essential, prednisone therapy may be continued with some reduction in dosage, but definitely with a strict ulcer regimen.

The appearance of glycosuria or an increase in severity of existing diabetes was noted in nine of our patients. In general, adherence to a diabetic regimen, or reduction in the dosage of prednisone, managed the situation.

Conclusions

As evaluated in a series of 156 patients with rheumatoid arthritis, prednisone appeared to be an effective agent in suppressing rheumatoid activity and in improving the functional capacity of the individual. In general, side-effects of therapy were not disturbing. However, disturbing gastrointestinal symptoms and signs did appear. Definite peptic ulcer was noted in 7 of 43 patients with dyspepsia in whom gastrointestinal x-rays were made because of digestive distress. In five additional patients either gastric hemorrhage or perforation of an ulcer developed.

When absolutely essential for maintenance of the patient's functional capacity or his self-sufficiency, it may be possible to continue administration of prednisone even in the face of peptic ulcer, if a strict ulcer regimen, including diet, antacids, and antispasmodics, is administered concomitantly. In the final analysis, evaluation of any given therapeutic program in rheumatoid arthritis requires individualization of therapy and follow-up of patients over a period of many years.

The enforced resort to steroids for the management of rheumatoid arthritis, despite the occurrence of side-effects, including peptic ulcer with its inherently serious complications, emphasizes the urgency for the development of more effective agents for patients in whom nothing else provides adequate improvement of disability.

500 Penn Ave. (22) (Dr. Stolzer).

This study was aided by a grant from the Anne L. and George H. Clapp Charitable and Educational Trust to the Western Pennsylvania Chapter of the Arthritis and Rheumatism Foundation.

The prednisone and prednisolone used in this study were supplied as Meticorten and Meticortelone by the Schering Corporation, Bloomfield, N. J., and as Deltra and Hydeltra by the Sharp & Dohme Corporation, Philadelphia.

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Priestley in the United States.—The home of Joseph Priestley has been acquired and is being restored to its original appearance by the Borough of Northumberland, Pennsylvania, U. S. A. This house, started in 1795 and completed in 1797, and owned for many years by the Priestley family, was purchased in 1920 by the Pennsylvania State University and presented this year (1956) to Northumberland. The home is of Georgian architecture, is in fine condition, and occupies an acre of landscaped ground near the Susquehanna River. Under the direction of the Priestley Memorial Association, the widow's walk, kitchen and laboratory are being restored to their original apearance and the rooms refurnished with American furniture of about 1800. The Association desires to gather all obtainable information on Priestley and on his American home. It would like to receive reprints of articles bearing on his work, and it welcomes correspondence with anyone interested in this matter; visitors are welcome. Correspondents should write to Mr. Lewis K. Rich, 464 Front Street, Northumberland, Pennsylvania. The Division of History of Chemistry of the American Chemical Society is cooperating with the Priestley Memorial Association in the restoration of Priestley's laboratory. To this end a committee including Sidney Edelstein, Claude K. Deischer and Wyndham Miles (chairman) has been constituted. The committee wishes to locate apparatus of Priestley's American period, with the view of acquiring them or having replicas made. It welcomes correspondence with anyone knowing the whereabouts of apparatus, and with scholars interested in this project; correspondence should be addressed to Dr. Wyndham Miles, Edgewood, Maryland.—News and Views, *Nature*, Nov. 24, 1956.

ZOXAZOLAMINE AND/OR CHLORPROMAZINE FOR MUSCLE SPASM

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Eight patients who had skeletal muscle spasticities due to spinal cord injuries received various combinations of four drugs, (1) zoxazolamine, (2) a placebo resembling zoxazolamine, (3) chlorpromazine, and (4) a placebo resembling chlorpromazine. Each patient's status with respect to muscular spasticities was evaluated objectively by observers who, like the patient himself, did not know which combination of drugs he was receiving at a given time. The dosages used were 500 to 1,000 mg. of zoxazolamine and 25 to 50 mg. of chlorpromazine, all given four times a day, and were sufficient to cause some side-effects (drowsiness, nausea) in six of the eight patients. These dosages did not, however, have any consistent effect on muscular spasticity in this series of patients.

It is well recognized that involuntary muscle spasm is one of the most disturbing sequelae in cases of injuries of the spinal cord which have produced transverse myelopathy. At the Institute of Physical Medicine and Rehabilitation of the New York University–Bellevue Medical Center, spasticity has been found to be the major deterrent to the physical rehabilitation of a large number of quadriplegics and paraplegics.

Cooper [1] has pointed out the great usefulness of subarachnoid alcohol block for the relief of spasticity in paraplegia. Like other destructive neurosurgical procedures for eliminating spasm, this is irreversible. For this reason, a drug which would relieve spasticity without jeopardizing return of motor function would be of inestimable value.

Recently, zoxazolamine (Flexin) has been shown to produce a flaccid paralysis of the limb musculature of animals.[2] Chlorpromazine (Thorazine) hydrochloride is said to act as a skeletal muscle relaxant.[3] Amols [4] states that zoxazolamine is a mild muscle relaxant for spastic conditions and that this effect is markedly increased by combination with chlorpromazine. He found that this combination of zoxazolamine with small doses of chlorpromazine afforded the best therapy as a centrally active muscle relaxant. Smith and associates [5] found zoxazolamine to be 85% effective in relieving muscle spasm in rheumatoid disease where the major disability was due to stiffness and aching. Abrahamsen and Baird [6] administered zoxazolamine to 28 children with the spastic form of cerebral palsy and in every instance found a decrease of muscle tone on passive flexion. Rodríquez-Gómez and associates [7] in a similar study found that 14 of 18 patients with spasticity resulting from injuries of the spinal cord showed objective relief of spasticity.

Method of Study

In view of the encouraging reports cited above, a clinical evaluation of these drugs was initiated at the Institute of Physical Medicine and Rehabilitation. In a double-blind study, patients with spasm ranging from moderate to severe were given zoxazolamine or zoxazolamine placebo and chlorpromazine or chlorpromazine placebo in different combinations and dosages. The drugs were ordered by code and at no time did any of the reporting personnel know the drug combinations the patients were receiving. We felt that the only practical means of evaluating the merit of an antispasm medication was to assess clinically both its subjective and its objective effect on the patient. Daily reports (table 1) were submitted by the patient, his resident physician, his nurse, his full-time or part-time attendant, physical therapists, occupational therapists, and instructors in activities of daily living. Personnel were assigned to each patient on a permanent basis for the duration of the study.

From the Institute of Physical Medicine and Rehabilitation, New York University-Bellevue Medical Center.

TABLE 1.—*Study of Spasms and Spasticity*

Patient		
Date		Hour
Observer		
General performance in activity (check one)	Good	
	Fair	
	Poor	
Number of spasms (Check one)	None	
	Occasional	
	Frequent	
	Constant	
Severity of spasms (Check one)	Mild	
	Moderate	
	Severe	

Comments (e.g., almost fell out of chair, could not ambulate because of spasms, patient's emotional status, alertness, etc.)

To be completed daily for each patient by supervisor of each activity for which he is scheduled. If patient is absent, please so indicate. Reports to be turned in to department heads daily.

Report of Cases

Eight patients were included in the study regarding the effect of zoxazolamine and/or chlorpromazine in ameliorating skeletal muscle spasticity due to spinal cord injuries.

CASE 1.—This 22-year-old male student suffered a vertebral fracture dislocation of T-10 and T-11 in an automobile accident on May 13, 1954. At laminectomy the spinal cord was found to be three-quarters transected. The patient was admitted to the

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Institute of Physical Medicine and Rehabilitation on Jan. 3, 1956, and was found to have complete motor and sensory loss below the level of the 10th thoracic dermatome. There was moderate spasticity of both lower extremities which interfered with ambulation in braces.

TABLE 2.—*Drugs and Dosage (Case 1)**

Date 1956		Side-Effects
5/17	500 mg. zoxazolamine placebo 25 mg. chlorpromazine	
5/23	500 mg. zoxazolamine 25 mg. chlorpromazine	Dizzy, drowsy
5/31	1,000 mg. zoxazolamine 25 mg. chlorpromazine	Dizzy, drowsy
6/ 4	500 mg. zoxazolamine placebo 25 mg. chlorpromazine	"Feels better"
6/ 6	1,000 mg. zoxazolamine placebo 25 mg. chlorpromazine placebo	
6/12	500 mg. zoxazolamine placebo	
6/24	Home	

* No decrease in spasm; all drugs given 4 times a day.

CASE 2.—This 33-year-old man sustained a vertebral fracture-dislocation in an automobile accident on Jan. 28, 1955. He was admitted to the Institute of Physical Medicine and Rehabilitation on March 24, 1955, with severe spasticity of all four extremities which virtually prohibited all efforts at rehabilitation.

TABLE 3.—*Drugs and Dosage (Case 2)**

Date 1956		Side-Effects
5/17	500 mg. zoxazolamine 25 mg. chlorpromazine	
5/23	1,000 mg. zoxazolamine placebo 50 mg. chlorpromazine	
5/31	1,000 mg. zoxazolamine 50 mg. chlorpromazine	
6/ 1	1,000 mg. zoxazolamine	Drowsy, heart
6/ 4	50 mg. chlorpromazine	burn, malaise, "out of sorts"
6/ 5	750 mg. zoxazolamine placebo 50 mg. chlorpromazine	Drowsy
6/ 6	50 mg. chlorpromazine placebo	Bright
6/11	50 mg. chlorpromazine placebo	Weak, tired
6/12	750 mg. zoxazolamine 50 mg. chlorpromazine placebo	Nauseated
6/13	750 mg. zoxazolamine	Still nauseated
6/14	50 mg. chlorpromazine placebo	
6/15	Cut all drugs	No nausea
6/18	Off study	
6/28	Intrathecal alcohol wash done, with relief of spasms in torso and lower extremities	

* No decrease in spasm; all drugs given 4 times a day.

CASE 3.—This 44-year-old man had pain in his back on Aug. 10, 1953, followed by paraplegia at a level of the 10th thoracic vertebra. Laminectomy revealed a large epidural abscess which was evacuated. There then developed muscle spasm below the level of the injury of such severity as to produce dislocation of the right hip. The following surgical procedures were subsequently performed for relief of pain and spasm: (1) Jan. 6, 1954, bilateral obturator neurectomy; (2) Nov. 30, 1954, right femoral nerve crush and partial section of right psoas; (3) Dec. 9, 1954, sectioning of the anterior and posterior roots of T-10 and T-11 and of the anterior roots of T-12 and L-1 and L-2; (4) Feb. 1, 1956, anterior rhizotomy from L-2 to L-5; (5) March 30, 1956, spinothalamic tractotomy; (6) April 16, 1956, posterior rhizotomy from T-9 to L-2, right. Despite these multiple surgical procedures, when the patient was admitted to the Institute of Physical Medicine and Rehabilitation on May 1, 1956, severe spasm in both lower extremities continued to impede rehabilitation.

CASE 4.—This 40-year-old man sustained a spinal cord injury in an automobile accident July 19, 1954, with resultant quadriplegia at the level of the fifth cervical vertebra. He was admitted to the Institute of Physical Medicine and Rehabilitation on March 16, 1956, and spasms were found to be severe in all four extremities and trunk. There was normal range of motion on those occasions when the spasm could be broken through. Spasticity was so severe as to preclude attempts at rehabilitation.

TABLE 4.—*Drugs and Dosage (Case 3)**

Date 1956		Side-Effects
5/17	500 mg. zoxazolamine	
5/23	1,000 mg. zoxazolamine	Nausea
5/28	No drugs	Nausea subsides
5/31	750 mg. zoxazolamine placebo	
6/12	750 mg. zoxazolamine	
6/14	Off study	

* No decrease in spasm; all drugs given 4 times a day.

CASE 5.—This 22-year-old male college student sustained a paraplegia at the level of the second thoracic vertebra after a bullet injury to the spinal cord in September, 1955. He was admitted to the Institute of Physical Medicine and Rehabilitation on March 20, 1956. Moderate spasticity of the lower extremities interfered with bracing and with transfer activities.

TABLE 5.—*Drugs and Dosage (Case 4)**

Date 1956		Side-Effects
5/17	500 mg. zoxazolamine placebo 25 mg. chlorpromazine	
5/23	1,000 mg. zoxazolamine 25 mg. chlorpromazine	
5/31	1,000 mg. zoxazolamine placebo 25 mg. chlorpromazine	
6/ 6	1,000 mg. zoxazolamine 25 mg. chorpromazine	
6/11	1,000 mg. zoxazolamine 25 mg. chlorpromazine	Sleepy, nausea
6/12	1,000 mg. zoxazolamine 25 mg. chlorpromazine	Epigastric distress, nausea, sleepy, short of breath
6/13	1,000 mg. zoxazolamine placebo 25 mg. chlorpromazine	Nausea disappears
6/26	1,000 mg. zoxazolamine 25 mg. chlorpromazine	
7/24	Home—refused alcohol wash	

* No decrease in spasm; all drugs given 4 times a day.

CASE 6.—This 45-year-old steel-foundry worker experienced the sudden onset of severe interscapular pain on Oct. 8, 1955, followed shortly by quadriplegia. Laminectomy disclosed a protruded intervertebral disk compressing the spinal cord between C-7 and T-1. Spasticity was marked in the trunk and both lower extremities upon admission to the Institute of Physical Medicine and Rehabilitation on April 10, 1956. It was impossible for therapists to overcome the spasm.

TABLE 6.—*Drugs and Dosage (Case 5)**

Date 1956	
6/26	1,000 mg. zoxazolamine
6/30	1,000 mg. zoxazolamine 25 mg. chlorpromazine
7/ 1	1,000 mg. zoxazolamine placebo 25 mg. chlorpromazine placebo
7/ 6	1,000 mg. zoxazolamine 25 mg. chlorpromazine placebo
7/14	Off study

* No decrease in spasm; no side-effects; all drugs given 4 times a day.

CASE 7.—This 65-year-old housewife noted the onset of an unsteady gait at the age of 50. This was followed by progressive weakness and spasms of both lower extremities. Upon ad-

TABLE 7.—*Drugs and Dosage (Case 6)**

Date 1956		Side-Effects
5/17	500 mg. zoxazolamine 25 mg. chlorpromazine	
5/23	500 mg. zoxazolamine placebo 25 mg. chlorpromazine	
5/31	1,000 mg. zoxazolamine 25 mg. chlorpromazine	Dizzy, sleepy
6/ 6	1,000 mg. zoxazolamine 25 mg. chlorpromazine placebo	
6/13	1,000 mg. zoxazolamine placebo 25 mg. chlorpromazine placebo	
7/ 1	1,000 mg. zoxazolamine 25 mg. chlorpromazine placebo	
7/14	Intrathecal alcohol wash done, with relief of spasms in lower extremities	

* No decrease in spasm; all drugs given 4 times a day.

mission to the Institute of Physical Medicine and Rehabilitation on April 7, 1956, the neurological findings were those of degenerative pyramidal tract disease compatible with a diagnosis of multiple sclerosis.

TABLE 8.—*Drugs and Dosage (Case 7)**

Date 1956		Effect on Spasm
5/17	500 mg. zoxazolamine placebo 25 mg. chlorpromazine	No change
5/23	500 mg. zoxazolamine 25 mg. chlorpromazine	Slight reduction
5/31	1,000 mg. zoxazolamine placebo 25 mg. chlorpromazine	Spasm worse
6/ 6	1,000 mg. zoxazolamine placebo 25 mg. chlorpromazine placebo	No change
6/12	500 mg. zoxazolamine 25 mg. chlorpromazine placebo	Slight reduction
6/21	Home	

* No side-effects; all drugs given 4 times a day.

CASE 8.—This 41-year-old woman sustained a right hemiplegia in March, 1953. For many years prior to this, she had been hypertensive. At the time of her admission to the Institute of Physical Medicine and Rehabilitation on April 30, 1956, there was severe spasm in the right upper and lower extremities which markedly limited rehabilitation efforts.

Summary and Conclusions

A clinical study, in which the double-blind method was used, was conducted to evaluate the effectiveness of zoxazolamine, zoxazolamine placebo, chlorpromazine, and chlorpromazine placebo in various combinations and dosages for the relief of spasticity. Among eight patients studied (six quadriplegics and paraplegics, one multiple sclerotic, and one hemiplegic as a result of a cerebrovascular accident), only the patient with multiple sclerosis benefited (table 10) from the administration of zoxazolamine and chlorpromazine. The results reported here indicate that zoxazolamine and/or chlorpromazine are not effective in ameliorating skeletal muscle spasticity due to spinal cord injuries.

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TABLE 9.—*Drugs and Dosage (Case 8)**

Date 1956		Side-Effects
5/17	500 mg. zoxazolamine 25 mg. chlorpromazine	
5/23	1,000 mg. zoxazolamine 25 mg. chlorpromazine	Nausea, dizziness
5/28	1,000 mg. zoxazolamine placebo 25 mg. chlorpromazine	
6/ 6	1,000 mg. zoxazolamine	
6/ 7	Off study	

* No decrease in spasm; all drugs given 4 times a day.

TABLE 10.—*Frequency and Severity of Spasm with Drug Combinations Used*

Case No.	Disability	Zoxazolamine and Chlorpromazine Frequency and Severity	Zoxazolamine and Chlorpromazine Placebo Frequency and Severity	Zoxazolamine Placebo and Chlorpromazine Frequency and Severity	Zoxazolamine Placebo and Chlorpromazine Placebo Frequency and Severity
1	Traumatic paraplegia	Unchanged	Drug combinations not used	Unchanged	Unchanged
2	Traumatic quadriplegia	Unchanged	Unchanged	Unchanged	Unchanged
3	Epidural abscess with paraplegia	Unchanged	Drug combinations not used	Unchanged	Drug combinations not used
4	Traumatic quadriplegia	Unchanged	Drug combinations not used	Unchanged	Drug combinations not used
5	Traumatic paraplegia	Unchanged	Unchanged	Drug combinations not used	Unchanged
6	Quadriplegia after spinal cord pressure	Unchanged	Unchanged	Unchanged	Unchanged
7	Multiple sclerosis	Decreased	Decreased	Unchanged	Unchanged
8	Cerebrovascular accident right hemiplegia	Unchanged	Drug combinations not used	Unchanged	Drug combinations not used

The zoxazolamine used in this study was supplied as Flexin by McNeil Laboratories, Inc., Philadelphia, and the chlorpromazine was supplied as Thorazine by Smith, Kline & French Laboratories, Philadelphia.

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SEGAL'S TUBELESS GASTRIC ANALYSIS WITH AZURE A RESIN COMPOUND

A SIMPLE PROCEDURE FOR SCREENING INDIVIDUALS WITH ACHLORHYDRIA IN A GASTRIC CANCER DETECTION PROGRAM

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Patients with achlorhydria and hypochlorhydria show a much greater disposition to gastric cancer. Further, the early detection of pernicious anemia presents a problem because of the plethora of proprietary hematinics. As an aid to cancer detection, the tubeless method of determining free hydrochloric acid in the stomach removes many of the previous inconveniences which have discouraged widespread use of this screening test. However, pyloric obstruction, impairment of small intestinal absorption, hepatic disease, and impairment of renal function may interfere with the accuracy of the test.

Patients with achlorhydria, the so-called gastric cancer precursor group,[1] can be identified with a high degree of reliability by the simple method of tubeless gastric analysis devised by Segal and co-workers,[2] using orally administered azure A resin compound. This compound, ingested orally, colors the urine blue or blue-green if free hydrochloric acid is present in the stomach at the time of the test. We have found that, of 100 subjects who had been demonstrated by one or more intubation procedures to have achlorhydria, 95 showed anacidity by this simple tubeless method and that, of the 34 patients with proved pernicious anemia in this group, all showed anacidity by the tubeless technique. The significance of this finding is that this tubeless method of gastric analysis offers a simple procedure for screening persons with achlorhydria in cancer-detection centers, hospitals, outpatient departments, and doctors' offices. Once achlorhydria is detected, one may then institute periodically such other well-known examinations for the diagnosis of early asymptomatic gastric cancer as x-ray, gastroscopy, and cytology, which are not now practicable for use on a wide-spread, routine basis in the general population.

The azure A resin compound consists of a highly purified carboxylic acid cation-exchange resin (Amberlite XE-96), in which a specific number of hydrogen cations have been replaced by azure A dye cations. In the presence of dilute hydrochloric acid, the process is reversed and the azure A cations are displaced by the hydrogen cations of the free hydrochloric acid. A significant quantity of azure A is displaced in hydrochloric acid solutions with a pH lower than 3, with maximum displacement at a pH of 1.5.[2] The azure A dye, so released, is then absorbed in the small intestine and excreted in the urine, coloring it blue or blue-green.

The azure A resin compound was first introduced by Segal, Miller, and Plumb, in 1955,[3] as an improvement over the tubeless method of gastric analysis with quinine carbacrylic resin, which Segal and his associates employed previously.[4] Similar encouraging results were then reported by us [5] and by McGowan and Stanley,[6] Galambos and Kirsner,[7] Sievers and Gieselman,[8] and Bolt.[9] Our present study deals with the series of 100 subjects with achlorhydria referred to above.

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Method

After at least an eight-hour fast, the patient swallowed a Levin tube, and a fasting gastric aspiration was obtained. Three hundred cubic centimeters of 5% alcohol was then administered into the stomach via the Levin tube, and gastric specimens were obtained at 15-minute intervals for a period of one hour. Each specimen was titrated for free and total acid by the usual routine method, with use of Töpfer's reagent and phenolphthalein as indicators. If free hydrochloric acid was absent, 1 mg. of histamine phosphate was injected subcutaneously, and two additional specimens were aspirated 15 and 30 minutes after the injection of histamine. These specimens were similarly titrated for free and total acid. Thirty minutes after the administration of histamine the Levin tube was removed without aspirating the stomach completely. The patient then voided, and this specimen was identified as the control urine. The patient was then given 2 Gm. of azure A resin compound orally with 150 cc. of water. At times an additional 50 to 75 cc. of water was allowed, to assure the ingestion of all of the insoluble azure A compound. Two hours later, the patient voided again and this specimen was identified as the test urine. This procedure was followed for 79 of the 100 subjects. These 79 patients included 31 with pernicious anemia.

The remaining 21 subjects comprised patients who were known to have achlorhydria by previous intubation studies. Only three in this group were patients with pernicious anemia. These 21 patients were not

subjected again to a gastric analysis by intubation on the morning of the azure A test. These patients reported with empty stomachs, and, after voiding the control urine, they were given 1 mg. of histamine phosphate subcutaneously. Immediately thereafter, the azure A resin compound was administered as described above; the test urine was collected two hours later.

Two standard solutions of azure A were employed for color comparison, those containing 0.3 and 0.6 mg. The former was prepared by the addition of 0.3 mg. of azure A dye to 300 cc. of distilled water and the latter by the addition of 0.6 mg. of the dye to 300 cc. of distilled water. Aliquots of 10 cc. of the respective standard solutions were then poured into test tubes, and these two standard solutions were used for color comparison.

The control and the test urine specimens of each subject were diluted with water to a volume of 300 cc. Aliquots of 10 cc. of each diluted urine specimen were poured into test tubes, and each specimen was acidified with 1 drop of 18% hydrochloric acid. The test tubes were then heated in a bath of boiling water for a period of 10 minutes, after which they were allowed to cool slowly to room temperature. The color of the two urine specimens were then compared with the colors of the two standard azure A solutions.

Results of Azure A Tests in 100 Patients Found by Intubation Technique to Have Achlorhydria

	Patients, Total No.	Negative*	Borderline Positive†	Positive‡	Correlation of Two Tests, %
Patients with pernicious anemia.....	34	34	...	...	100
Patients without pernicious anemia.....	66	61	3	2	92
Total	100	95	3	2	95

* No change in color or color less than 0.3-mg. standard solution of azure A.

† Color equal to or more intense than 0.3-mg. standard but less intense than 0.6-mg. standard solution.

‡ Color equal to or more intense than 0.6-mg. standard solution.

It might be added that the 100 subjects in this series comprise a selected group of patients—selected, in that they failed to show free hydrochloric acid during one or several intubation tests. We concentrated on subjects with achlorhydria, because we were particularly interested in determining whether the azure A resin compound test is sufficiently accurate to warrant its use in the screening of subjects with achlorhydria, in whom the incidence of gastric cancer is high.

We excluded from this study patients known to have pyloric obstruction, impairment of small intestinal absorption, hepatic disease, or impairment of renal function and patients with urinary retention, since these conditions might interfere with the accuracy of the azure A test.

Interpretation of Results

In interpretation of the results, if the test urine specimen developed a blue color equal to or more intense than that of the 0.6-mg. standard solution, the test was interpreted as positive, i.e., as showing that the subject has secreted free gastric hydrochloric acid. If the test urine specimen developed a blue color ranging in intensity from that of the 0.3-mg. standard to less than that of the 0.6-mg. standard, the test was interpreted as positive, but borderline, i.e., as showing that the subject did secrete free gastric hydrochloric acid but that it was probably of low hydrochloric acid concentration. If the test urine specimen failed to develop a blue color or developed a bluish color of less intensity than that of the 0.3-mg. standard, the test was interpreted as negative, i. e., as showing that the patient did not secrete free hydrochloric acid at the time of the azure A test. These interpretations were employed by us in our previous study of 114 patients, in each of whom both the intubation method of gastric analysis and the tubeless azure A method were employed during the same morning.[5] We found 95% accuracy with the tubeless method, when the results were compared with those of the intubation technique.

Results

Details of the results are given in the table. It will be noted that the azure A test was negative in each of the 34 patients with pernicious anemia, a correlation of 100%. Of the 66 patients without pernicious anemia who were found to have achlorhydria on one or more intubation tests, 61 showed negative azure A tests, a correlation of 92%. Three patients showed positive but borderline tests, and two showed definitely positive azure A tests. In three of these five patients both the intubation and tubeless tests were repeated with similar discrepancy in the results. Of the 5 patients in whose specimens free hydrochloric acid was shown to be present on azure A tests, 3 were among the 79 on whom the two tests were performed during the same morning (4% failure of correlation) and 2 were among the 21 on whom the two tests were performed during different days (10% failure of correlation). Of the total series of 100 subjects whose specimens failed to show free hydrochloric acid when tested by the intubation technique, 95 failed to show hydrochloric acid secretion on the azure A test, giving an over-all correlation of 95%.

Comment

The 34 patients with proved pernicious anemia definitely had true achlorhydria. In this group of patients, the azure A tests were all negative, a correlation of 100%. It is unlikely, however, that the 66 patients without pernicious anemia all had achlorhydria, since it is well known that failure to find free hydrochloric acid in one or two series of fractional gastric analyses does not necessarily prove true achlorhydria, even though effective doses of histamine are used. This might explain the positive results on the azure A test in five of the patients. These five patients might well be found to be acid secretors on repeated intubation tests, as

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was the case with several patients not included in this series. Consideration should also be given to a possible displacement of the azure A cations by hydrogen cations of the acid contents of the small intestine; this might account for an occasional positive azure A test among patients who have true gastric achlorhydria. This might also explain the voiding of blue-colored urine for a day or two after the azure A test, which occurred even among some of our patients with pernicious anemia.

As stated above, the 66 subjects without pernicious anemia, although they failed to show free hydrochloric acid on one or two intubation tests, do not necessarily have true achlorhydria. The same can be said for those whose specimens failed to show hydrochloric acid on the azure A test. In fact, we question whether the azure A test can be depended upon for a diagnosis of true achlorhydria, especially since the azure A cations are displaced by the hydrogen cations at a pH of only 3.[2] To prove true achlorhydria, patients would have to be subjected to repeated intubation studies, employing also other gastric secretory stimulants besides alcohol and histamine.[10] Also, it would be essential to determine the pH values for each of the gastric specimens studied.[10a] No doubt a number of these 66 subjects would be found to be acid secretors if such procedures were employed. We did not consider such a program essential for the present study, however, because we were interested primarily in determining the degree of correlation between the azure A test and the intubation test, which is generally in use, and in determining whether the azure A test is sufficiently accurate to warrant its use in a gastric cancer detection program in the screening of patients with both achlorhydria and hypochlorhydria, since each group has a greater disposition to gastric cancer. If it is assumed, as we believe that it can be assumed, that most of these 66 subjects who were shown to have achlorhydria by intubation tests have either achlorhydria or hypochlorhydria, then, indeed the 61 individuals with negative results and the 3 with borderline results on the azure A test are those who should be screened for subsequent careful and thorough study.

The greater disposition of patients with achlorhydia and hypochlorhydria to gastric cancer is well known. Recently Hitchcock and co-workers [1] reported that the incidence of gastric cancer in this group is 5.2 times higher than would be expected in a similar age group in the general population. These authors employed the intubation method of gastric analysis, employing histamine as the gastric secretory stimulant. The even greater disposition of patients with pernicious anemia to gastric cancer is also well known. The same authors reported that, in patients with pernicious anemia, the incidence was 18.3 times higher. Other studies indicate that gastric cancer is found once in each 100 patients with gastric anacidity; in patients with pernicious anemia, the incidence of gastric cancer may be as high as 3 to 5 per 100 patients examined.[11] Depending on the sample selected, Zamcheck and coworkers [12] found that the frequency of gastric cancer among patients with pernicious anemia varied from less than 1% to more than 11%. It might be added that the early detection of pernicious anemia also presents a problem nowadays because of the plethora of proprietary hematinics, which mask many cases of pernicious anemia.

The great inconvenience of and the time required by the intubation method of gastric analysis have discouraged the test's widespread use as a screening device for identifying patients with achlorhydria. With the tubeless method, these deterrents are absent. The following conditions, however, may interfere with the accuracy of the azure A test: pyloric obstruction, impairment of small intestinal absorption, hepatic disease, and impairment of renal function.

Of course, it is well known that gastric cancer occurs also among individuals with normal values of free gastric hydrochloric acid. We are of the opinion, however, that an aggressive program of cancer detection among persons with achlorhydria and hypochlorhydria, in whom the incidence of gastric cancer is high, would certainly be a step in the right direction. As a first step in this program, it is recommended that the azure A tubeless method of gastric analysis be instituted as a routine screening procedure in cancer-detection centers, hospitals, outpatient departments, and physicians' offices. Once achlorhydria or hypochlorhydria is detected, the patients may then be subjected regularly to the other well-known examinations for the detection of early asymptomatic gastric cancer, such as x-ray, gastroscopy, and cytology. Such a program is now in operation in the outpatient department at Harper Hospital, Detroit, for all patients 40 years of age and older.

Summary

One hundred subjects found to have achlorhydria by the intubation method of gastric analysis were subjected to Segal's tubeless method of gastric analysis, with use of the orally administered azure A resin compound, which colors the urine blue or blue-green when free hydrochloric acid is present in the stomach. Alcohol and histamine phosphate were used as the gastric secretory stimulants. Thirty-four of the subjects were patients with proved pernicious anemia. Seventy-nine of the patients were subjected to the two tests during the same morning and 21 patients on different mornings.

Of the 34 patients with pernicious anemia, all showed negative results on the azure A test—a correlation of 100%. Of the 66 subjects without pernicious anemia, 61 showed negative results on the azure A test— a correlation of 92%. Three patients showed positive but borderline results, and two patients had definitely positive results. Of the 5 patients who failed to show correlation between the two tests, 3 were among the 79 patients on whom the two tests were performed during

the same morning (4% failure of correlation) and 2 were among the 21 patients on whom the two tests were performed on different days (10% failure of correlation). Of the total 100 subjects, 95 showed negative results on the azure A test—an over-all correlation of 95%.

Our data indicate that Segal's tubeless method of gastric analysis with azure A resin is sufficiently accurate to warrant its use in screening patients for achlorhydria and hypochlorhydria, in whom the incidence of gastric cancer is known to be high. Once these conditions are detected, the other well-known examinations for the detection of early asymptomatic gastric cancer, such as x-ray, gastroscopy, and cytology, which are not now practicable for use on a widespread routine basis in the general population, may then be instituted and used periodically.

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The azure A resin compound used in this study was supplied by E. R. Squibb and Sons, New York.

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SOLOX INTOXICATION

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Severe hypoglycemia from any cause is a grave medical emergency because of the rapidity with which irreversible cerebral damage or death may ensue. It is, thus, of the utmost importance to diagnose and treat this condition correctly and rapidly. Solox "smoke" intoxication is a relatively common cause for profound hypoglycemia, but the condition frequently appears under circumstances tending to obviate the recognition of that hypoglycemia. Solox is the trade name for a shellac solvent made according to the following formula: pure ethyl alcohol, 100 gal.; denatured grade wood alcohol, 5 gal.; gasoline, 1 gal.; ethyl acetate, undenatured, 1 gal.; methyl isobutyl ketone, 1 gal. Brown and Harvey [1] in 1941 reported six patients who were brought to Johns Hopkins Hospital in hypo-

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Solox is the trade name for a shellac and paint solvent consisting primarily of ethyl alcohol and methanol. The clinical picture of Solox intoxication, by ingestion, is coma, a foul chemical odor to the breath (similar to wood alcohol with a superimposed, sweetish, acetone-like overtone), acidosis, and, of particular importance, hypoglycemia. There is a peculiar extensor rigidity of the extremities, apparently correlated with the hypoglycemia. Therapy is usually toward correcting the acidosis, alleviating the hypoglycemia, preventing complications, and giving supportive care. Recovery is complete if death does not intervene.

glycemic coma after drinking what was believed to be a liquid paint remover. Tucker and Porter [2] reported four similar cases in 1942 and stated, "It is well known that a preparation sold under the name of 'Solox' is widely used in the Richmond (Va.) area as a beverage." Bennett [3] has observed Solox intoxication to be a frequent occurrence in the southern states.

The exact number of patients brought to a hospital with Solox intoxication cannot be obtained. A history is usually not available, and the frequent emergency treatment of alcoholism with intravenous injection of hypertonic dextrose solution may alleviate the hypoglycemia. Because this disorder is not widely recognized, most of these individuals are treated only in the emergency wards and are never admitted to the hospital.

Selection of Patients

This study consists of patients seen in the admission rooms or admitted to the wards of both the University Hospital and the Veterans Administration Hospital, Birmingham, Ala., from 1946 to 1956. Thirty-six patients either gave a history of drinking Solox or presented a clinical picture typical enough to be diagnosed as such. All but four of these were Negroes, and the majority had been chronic alcoholics for several years. The purpose of this paper is to present and discuss the effects of Solox intoxication in these patients and to emphasize the hypoglycemia which is frequently present. Severe acidosis, methanol poisoning, or hypoglycemia necessitated hospitalization of many of these patients, and death was a frequent occurrence. It was considered likely that 15 other patients had consumed this mixture, but the data were not conclusive enough to merit their inclusion in this series. The figure presents certain clinical and laboratory findings of these patients.

Clinical Picture

An immediate history is seldom obtained from these patients because they are usually comatose. History obtained subsequently from relatives or friends reveals that chronic alcoholism has usually been present, with a degree of malnutrition and starvation compatible with the extent of the alcoholic debauch. Solox intoxication and acute ethanol intoxication are so similar that very few patients are brought to the attention of physicians unless coma or other complications occur which necessitate emergency care. Occasionally, when the patient is conscious, he may complain of blurred vision, intense cramping abdominal pain, and burning of the eyes. The abdominal pain is often relieved by intravenously administered hypertonic dextrose solution. The odor of the breath is characteristic, but it is difficult to describe. There is a foul, chemical odor, similar to wood alcohol, with a superimposed, sweetish, acetone-like overtone. It is distinctly different from, and should not be confused with, the acetone odor of diabetic acidosis.

CASE #	AGE	SEX	RACE	SOLOX HISTORY	PUPILS	REFLEXES	SHOCK	RESP	EXTENSOR RIGIDITY	(mgm/%) BLOOD GLUCOSE	(meq.) BLOOD CO_2	OUTCOME
1	39	♂	N	—	?	DTR ↓	BP $\frac{88}{58}$	?	?	?	?	DIED
2	40	♂	N	+	Dilated Fixed	NORMAL	—	8/min.	?	?	?	DIED
3	60	♂	N	—	Dilated Fixed	NORMAL	—	10/min.	?	?	?	DIED
4	45	♂	N	1 quart	Dilated Fixed	ABSENT	—	Normal	Present	?	?	DIED
5	38	♂	N	+	?	?	BP $\frac{68}{0}$	14/min.	?	?	?	DIED
6	21	♂	N	½ pint	Dilated Fixed	Normal Arms Absent Legs	—	60/min.	—	?	17.2	DIED
7	39	♂	N	Solox on Breath	Dilated Fixed	ABSENT	—	24/min.	—	?	?	Recovered
8	40	♂	W	2 quarts	Normal	?	—	16/min.	—	?	?	Recovered
9	34	♀	N	?	?	?	?	12/min.	?	?	?	DIED
10	49	♂	N	+	Dilated Fixed	↓ DTR Babinski	BP $\frac{84}{70}$	32/min.	?	?	?	DIED
11	?	♂	N	+	?	?	BP $\frac{0}{0}$	8/min.	—	?	?	DIED
12	35	♂	N	Solox on Breath	Dilated Fixed	NORMAL	—	20/min.	?	?	?	Recovered
13	43	♂	N	+	?	?	—	—	?	?	?	Recovered
	same patient			+	Normal	DTR ↓	—	—	?	?	15	Recovered
14	47	♂	N	?	VARIABLE		—	40/min.	Present	31	15.5	Recovered
15	29	♀	N	+	Normal	—	—	18/min.	?	117	?	Recovered
16	65	♂	N	?	?	?	BP $\frac{80}{20}$	?	?	63 next day	?	Recovered
17	32	♂	N	?	Small Fixed	?	BP $\frac{78}{0}$	10/min.	?	19	22	DIED
18	4	♂	N	?	?	ABSENT	BP $\frac{40}{0}$	10/min.	—	38	11	Recovered
19	46	♀	N	pint $\frac{3}{4}$	Normal	NORMAL	—	—	?	13 17	13.2 12.3	Recovered
20	44	♂	N	+ 10 Years	VARIABLE		shock 4 days	variable	Present	?	6.8	Recovered
21	37	♀	N	?	?	Babinski DTR ↓	—	40/min.	Present	23	15	Recovered
22	5	♂	N	? +	Dilated Fixed	Babinski DTR ↓	?	?	Variable	99	12 15	Recovered
23	44	♂	N	+	?	?	BP $\frac{80}{40}$	?	?	?	?	Died Pneumonia
24	42	♂	W	+	?	?	?	?	?	?	?	Recovered
25	39	♂	N	+	?	?	?	?	—	92	20	Recovered
26	?	♂	N	+	Variable	DTR ↓	BP $\frac{94}{48}$	?	—	?	?	Recovered
27	42	♀	N	odor of breath	?	?	BP $\frac{90}{0}$	34/min.	?	?	?	DIED
28	32	♂	N	+	Dilated React	NORMAL	—	18/min.	—	?	?	Recovered
29	49	♂	N	+	DID NOT COME TO HOSPITAL					?	?	Recovered
30	51	♂	N	±	Normal	DTR ↑	—	20/min.	Present	27 33	20.3	Recovered
31	30	♂	N	+	DID NOT COME TO HOSPITAL					?	?	Recovered
32	47	♂	W	+	DID NOT COME TO HOSPITAL					?	?	Recovered
33	49	♀	N	+	?	"Abnormal"	BP $\frac{100}{60}$	?	Variable	90	?	DIED
34	46	♂	N	+	Dilated React	DTR ↓	—	18/min.	—	?	19.3	Recovered
	same pt	SAME		+	"	DTR ↓	—	18/min.	—	—	—	Recovered
35	34	♂	W	+	Normal	DTR ↓	—	—	?	105	18.9	Recovered
36	37	♂	N	+	Normal	Normal	—	16/min.	—	66 75	19.5	Recovered

Clinical and laboratory findings of 36 patients suffering from Solox intoxication. Blood and cerebrospinal fluid determinations were by method of Folin and Wu. Carbon dioxide–combining power was determined by the method of Van Slyke. DTR = deep tendon reflexes.

On physical examination the blood pressure and pulse are usually normal unless an injury has been sustained. The respirations may be deep and rapid or shallow and depressed, depending on the state of narcosis. Despite laboratory evidence of severe acido-

sis, some patients have normal respirations, but during recovery a transient period of hyperpnea may develop. The neurological picture is bizarre and changes during the course of the illness. There is often extreme irritability of the central nervous system as manifested by mania and convulsions in the less comatose patients. The pupils are usually widely dilated and fixed; anisocoria may also be present. The importance of the possibility of intracranial injury becomes evident, and this must be excluded by skull films, neurological examination, and careful observation during the intoxicated phase. The gag and cough reflexes are frequently diminished so that aspiration of vomitus occurs. Generalized flaccidity may be observed, with no deep tendon reflexes obtainable; however, this may alternate with extensor rigidity of the extremities if hypoglycemia is present. The response to pain is diminished over the entire body. Pathological reflexes may or may not be present. Bilateral Babinski reflexes have been observed to revert to normal as recovery occurs.

Examination of the lung fields often reveals evidence of pneumonitis. In such instances, numerous rales are heard on auscultation, and they simulate acute pulmonary edema. Digitalization may become necessary as a precautionary measure because acute cardiac decompensation frequently cannot be excluded clinically. This picture is also seen in other hydrocarbon ingestions such as gasoline, kerosene, and petroleum oils. Laboratory evidence of a mild to severe acidosis usually is present, with a carbon dioxide–combining power much lower than the clinical picture would suggest. The blood sugar level may be normal or markedly decreased, with concentrations as low as 13 to 17 mg. per 100 cc. The extensor rigidity of the extremities is apparently correlated with the hypoglycemia. Blood ketones have been observed to be 60 times normal, with blood lactate 8 times normal during the acute intoxication phase. Acetonuria has been present in many of these patients, but never as marked as in diabetes mellitus. Despite the bizarre neurological picture, the cerebrospinal fluid findings are not remarkable; however, no lumbar punctures were made during the hypoglycemic phase.

The course of the illness is variable and depends upon the individual response to the relatively small amount of methanol, and to other complications such as trauma, aspiration of vomitus, and intercurrent disease. Most of these patients are never seen at a hospital and presumably recover without treatment. Death is infrequent in patients who are treated promptly, but chronic mental and physical degeneration may accompany repeated episodes of intoxication.

Pathological Findings

Ten autopsies have been performed at the University hospital on patients believed to have ingested Solox prior to death. Chemical tests, when performed, have demonstrated ethanol and methanol in all tissues, especially the brain, kidneys, and liver. Fatty change of the liver, generalized congestion of all organs, and pulmonary and cerebral edema have been the most frequent findings at autopsy. Three patients have shown pancreatic hemorrhages, but these changes could not be correlated with the hypoglycemic picture, as blood sugar determinations were not done prior to death. The pathological changes represent those found with combined ethanol and methanol intoxication but give no insight into the mechanism of the hypoglycemia.

Treatment

Therapy has usually been directed toward correcting the acidosis, alleviating the hypoglycemia, preventing complications, and giving supportive care. Sodium lactate solution has been used intravenously with success for the acidosis. As a high blood lactate level has been noted during the acute phase, it may be better to use a 2% solution of sodium bicarbonate. Hypertonic dextrose solution given intravenously at 4-to-6-hour intervals for the first 24 hours will usually correct and prevent a recurrence of the hypoglycemia. Patients should be observed carefully for 24 hours after ingestion of Solox because of the frequent recurrence of the hypoglycemia at any time during this period.[4] With prompt diagnosis and treatment, the death rate declines (see figure). Pneumonia has been a frequent complication, and it is advisable to use antibiotics prophylactically and to do a bronchoscopy, if aspiration has occurred. Intravenous therapy with levarterenol or other pressor agents may become necessary, but usually shock is associated only with concurrent injuries.

Comment

Solox intoxication is seen rather frequently in large city hospitals. The clinical picture is so variable that the diagnosis may not be made unless the syndrome is remembered each time a comatose alcoholic is seen. Coma, chemical odor to the breath, hypoglycemia, extensor rigidity of the extremities, unequal deep tendon reflexes, and abnormal reflexes may be seen. As with methyl alcohol, there apparently is a great individual variability of response. All members of a group may drink the same amount, but only a few will develop toxic symptoms. Prolonged usage without any demonstrable ill-effects is very common. Patients have admitted consuming this substance almost each weekend for a period of 10 years without evidence of damage determined by physical examination or laboratory procedures. Although Bennett [5] and Brown and Harvey [1] observed no patients with severe acidosis, patients have been seen in this series with carbon dioxide–combining powers as low as 3.8 mEq. per liter. All of the patients observed with hypoglycemia have been acutely intoxicated in contrast to reports by Tucker and Porter [2] who observed this complication in patients who had slept overnight.

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The peculiar extensor rigidity of the extremities is apparently correlated with the hypoglycemia. A similar reaction is often observed in patients with insulin hypoglycemia and hypoglycemia associated with other diseases, such as the "vomiting sickness of Jamaica," which has been reported by Jelliffe and Stuart.[6] The clinical picture of the vomiting sickness is identical to Solox intoxication and is thought to be due to ingestion of toxic wild berries of the genus Blighia sapida. Hypoglycemia, extensor rigidity, coma, convulsions, and death may occur with this syndrome. Recovery is complete if death does not intervene. A liver biopsy performed on one of these patients revealed almost complete absence of liver glycogen. Hassall and others[7] isolated polypeptides from the berries of Blighia sapida and found that these will cause experimental hypoglycemia in animals. The have called these substances hypoglycin A and B. The effect of these compounds on liver glycogen and blood sugar was more than doubled when starvation was present.

The cause of hypoglycemia in Solox intoxication is not known. Intoxication produced experimentally with Solox in normal and starved dogs by Brown and Harvey,[1] and an extensive series of tests on rabbits by Bennett[3] have failed to produce hypoglycemia. The animals were kept comatose for hours, but the result was narcosis only.

There has been no evident hepatic disease to account for the hypoglycemia in the patients in this study. However, in view of the marked glycogen depletion seen in the vomiting sickness of Jamaica, it is obvious that this may be a contributing factor. Malnutrition resulting from the use of alcohol as a food substitute may prepare the liver so that the normal conversion of glycogen to glucose cannot occur as rapidly as is necessary for homeostasis.

Selective poisoning of enzyme systems in the liver is another possibility, although it seems unlikely because of the rapid and complete reversibility of the process. Lesions of the central nervous system have been known to be associated with hypoglycemia, and it is interesting to speculate on a similar irritative effect of Solox. There is nothing clinically or experimentally to substantiate this, however. Evans and co-workers[8] have reported that disruption of sympathetic impulses to the liver of a cat can cause hypoglycemia.

Although occasionally ethanol intoxication alone may be associated with spontaneous "functional" hypoglycemia and hyperventilation syndrome,[9] none of the constituents of Solox do this frequently. Gasoline intoxication may cause tonic muscle spasm, thereby simulating the extensor rigidity. The other constituents either alone or in combination are known to produce cerebral and pulmonary edema, narcosis, coma, and convulsions. Pathologically, these compounds cause fatty change in the liver and kidneys, as well as generalized congestion of all organs.

A majority of the clinical and pathological manifestations are explained by a study of the toxicity of the individual constituents. However, the origin of the frequent and severe hypoglycemia remains obscure. Any of the known causes of hypoglycemia discussed in this paper or possibly unknown homeostatic mechanisms may be involved. The difficulty of study of such patients is obvious, and the rapid treatment necessarily precludes adequate investigation of the hypoglycemia.

Summary

Intoxication with a paint solvent called Solox has been seen frequently in several southern states. A study was carried out of 36 patients with this condition seen at the University Hospital or the Veterans Administration Hospital, Birmingham, Ala. Coma, chemical odor to the breath, acidosis, and hypoglycemia characterize the syndrome. Death may occur as the result of methanol poisoning, respiratory depression, or complications such as aspiration pneumonia. Autopsy findings have been nonspecific. The mechanisms of the hypoglycemia is not understood and most attempts to reproduce hypoglycemia in animals have failed. The syndrome is similar to the "vomiting sickness of Jamaica," in which a toxic hypoglycemia follows ingestion of wild berries.

Addendum

Since the writing of this paper, a patient has been observed with a blood glucose level of 12 mg. per 100 cc. and cerebrospinal fluid sugar level of 10 mg. per 100 cc. This emphasizes the severity of the hypoglycemia to which the central nervous system is subjected.

The formula for Solox was given by U. S. Industrial Chemicals Company, New York City.

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HEMATOLOGY—RECORD OF A CENTURY: 1856-1956

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One hundred years ago the word anemia was in use, although few measurements of blood had been performed. Purpura and plethora were classified, but there were few, if any, supporting laboratory studies. Blood cells were examined in the fresh state without staining, and blood cell counting was just beginning. Fifty years ago, reduced platelets were described in connection with purpura hemorrhagica, and the blood groups were discovered. A little over a quarter of a century ago, the effects of liver in pernicious anemia opened wide the newer hematology, in which pathophysiology was emphasized. At present we are at the beginning of the era of hematological chemistry. This will undoubtedly lead to expansion in the fields of coagulation disorders, immunohematology, and the hemoglobin abnormalities. The prevention of useless blood loss and the conservation of this most precious fluid for an increasingly healthy society must be the constant aim of the world-wide fraternity of hematologists.

As we meet here in this, the 10th year of our society, and at what I am sure is the largest single world-wide gathering of hematologists ever held, it is well to reflect for a while on hematology as it was, as it is now, and what it might become in the not too distant future. What hematology in all its complexity has become can be seen by a quick glance through our voluminous program, but, lest we feel smug at all our knowledge, let us mention but a few names—leukemia, hemophilia, paroxysmal nocturnal hemoglobinuria (PNH)—and we are immediately aware of how little we actually know of these and other equally mysterious states. Still, the 100 years immediately behind us have witnessed an enormous advance in hematology, certainly as rapid as in other fields of medicine, and perhaps more so than in most.

In 1856, the word anemia was in use, although as yet very few actual measurements of the blood had been performed. Just the preceding year, Addison had first used the designation of "idiopathic" anemia. Although Addison's descriptions of what we know now as pernicious anemia were of some accuracy, it is curious that he chose to bracket his descriptions of the anemic disease with those of the suprarenal capsule. Also in 1855, Virchow first accepted the term leukemia, after his original description of "Weisses Blut," and this name has stuck. Purpura and plethora, conditions of ancient lineage, were classified and subclassified; but without laboratory studies, little progress could be made. For all of these conditions, even for many cases of anemia, "bleedings" were performed as an important means of therapy. In chlorosis, the "green sickness," however, Sydenham the English clinician (1624-1689) and later Pierre Blaud in 1832 used large doses of iron with excellent results.

In 1856 the place of the laboratory in hematological studies was primitive indeed. Blood cells were examined in the fresh state without staining; blood cell counting was just beginning (Vierordt, Welcker). But, in the next two decades, great strides were made. First, there was the development of hematometry (Potain, Malassez, Gowers, Hayem). Later came the introduction of analine dye staining techniques by that great genius, the father of hematology whose 100th birthday we celebrated two years ago, Paul Ehrlich. May I quote from an editorial of mine published in *Blood* two years ago:

> The impact of Ehrlich's discovery and its widespread effects on many fields cannot of course be assessed, but it was certainly considerable. It is illustrative of the importance of the development of a method—for this simple staining technic made possible the study of many different kinds of blood cell reactions, including those found in infections, in the different types of anemia, and in leukemia. In the blood, he devised differential counting, made sharp distinctions between the various types of leukocytes and their granules, described polychromatophilia and poikilocytosis, and pointed to the close relationships existing between the blood picture and the bone marrow.
>
> For the first time the marrow could be adequately stained and carefully studied. Here, Ehrlich described the myelocyte, which he considered as the precursor of the granulated white cells of the blood; the megaloblast of pernicious anemia, which he distinguished from the normoblast; the mast cell; and the fatty picture of aplastic anemia.

There can be no question of the enormous effect the introduction of these two rather simple methods, cell counting and cell staining, had on the development of hematology. It was now possible to recognize and describe all manner of "new" diseases, previously "hidden" from view. Hematology threw off its colorless shackles and dazzled its devotees with Ehrlich's reds, blues, and violets; sometimes too much so, to judge by the lengthy polemical articles that were written by such masters as Pappenheim, Nägeli, and their contemporaries.

By 1900, hematology was well on its way. In Ehrlich and Lazarus' textbook, published at the turn of the century, there were large chapters on normal and pathological physiology of the blood, simple chronic anemia, progressive pernicious anemia, chlorosis, acute lymphatic leukemia, chronic lymphatic leukemia, pseudoleukemia, and myeloid leukemia. Hayem went further. His textbook "Du Sang," published in 1889, and his "Leçons" of 1900, did more to put hematology

Presidential address, read before the sixth Congress of the International Society of Hematology, Boston, Aug. 29, 1956.

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on a firm basis than almost anything else. It was easy to see how far ahead of his time was this little giant who trod the Parisian scene for so many years. His descriptions of purpura hemorrhagica, in which for the first time he noted that the platelets (hematoblasts) were greatly reduced; his discussions on paroxysmal hemoglobinuria, cyanosis, hyperglobulia, and other subjects are just as fresh now as they were when they were written 56 years ago. In 1900, too, Landsteiner, then a Viennese, while working in the old Allgemeines Krankenhaus, made his epic discovery of the blood groups and before that, with Donath, was the first to find an autohemolysin in paroxysmal hemoglobinuria.

Advances in Hematology in the Twentieth Century

It was an auspicious beginning for the new century. Hemolytic anemia was first distinguished and studied extensively by various groups in Paris and Italy. Here in America Herrick, in 1910, first described sickle cell anemia. Banti focused his attention on the spleen as a hemolytic and "noxa"-producing organ and was the first (with Micheli) to recommend splenectomy as a therapeutic procedure. In 1916 Kaznelson instituted splenectomy for idiopathic thrombocytopenic purpura. Experimental and physiopathological hematology were beginning. Transfusions, based on Landsteiner's principles of blood grouping, began to be used, particularly when citrate was introduced as an anticoagulant by the Argentinian Agote in 1915 and by Lewisohn in New York (1914-1916). Leukemia was treated first by chemicals (arsenic, benzol) but later by x-rays, radium, and mesothorium.

By 1923, hematology was a rather dull, but respectable specialty: in some areas dominated by the pathologists; in some, as in New York, by the transfusionists; and here in Boston by the clinicians. We had here at that time Richard C. Cabot, whose horizons had already extended beyond hematology; James Homer Wright of megakaryocyte-platelet fame; and George R. Minot. Minot was fundamentally a clinician but at the same time an investigator. He believed passionately in clinical investigation; i. e., noting the problem in the patient, taking it to the laboratory for experimentation, bringing back the findings of the laboratory for further enlightenment in the clinic. With James H. Means, he talked to us constantly at school of the pathological physiology of disease and alluded only briefly to the morphologic aspects of the blood cells, so beloved by the European hematologists. Whipple's experiments indicating the remarkable effects of liver in the hemorrhagic anemia of dogs led Minot to try this substance in pernicious anemia with the almost incredible results all of of you know so well. This may be said to have opened up and revitalized the whole field of hematology, so that now its rate of advance became well-nigh phenomenal.

Castle's studies of the "conditioned" deficiency state of pernicious anemia led the way in the new pathophysiology of hematology. The hemolytic diseases opened up; at first the immunological forms: autoimmune and iso-immune; later, the pathophysiology of the hereditary forms, spherocytosis and sickle cell disease, were investigated. A rare mysterious disease, paroxysmal nocturnal hemoglobinuria, opened up all kinds of new vistas in intravascular blood destruction, iron deposition and excretion, the effects of plasma constituents on the abnormal red blood cells of the disease, and many other fascinating subjects. Polycythemia with its numerous manifestations, multiple myeloma with the many abnormalities due to the abnormally high plasma globulins, even the leukemias—all became subjects for intensive studies in the pathological physiology of disease.

With the introduction of corticotropin (ACTH) into the clinic, even such a prime morphologic favorite as the eosinophil became involved in the endocrine

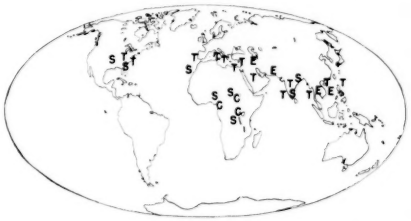

Fig. 1.—The "geohematology" of the hemoglobinopathies. T=thalassemia, S=sickle cell disease, C=hemoglobin C disease, E=hemoglobin E disease. The abnormal hemoglobins and the associated diseases are found in a broad central band of countries around the world and usually in people with some type of skin pigmentation, brown to black.

sphere. The concept of an erythropoietic hormone was revived, and humoral regulation of the lymphoid and splenic tissue became subjects of lively discussion.

In the field of the leukemias and the white blood cell tumors (leukosarcomas), chemotherapy in the form of radiomimetic chemicals (notably nitrogen mustard) and of antimetabolites in the form of analogues of vitamins (notably the folic acid antagonists) held promise of the eventual control of these dread neoplastic conditions. Newer methods for studying the disordered blood cells, such as electron microscopy, phase microscopy, histochemistry, and time-lapse cinematography, opened up new vistas in the old field of morphology and linked the histology of the cell with its physiology. However, as newer insights into disordered function were developed, it became more and more evident that it was essential to study the actual chemical changes which took place in cells, tissues, plasma, excretions—in other words, the whole metabolism of a process, not alone its disordered physiology.

Iron, desoxyribose nucleic acid, ribonucleic acid, the various protein constituents of blood, and the coagulation factors, to mention but a few, were intensively studied. The radioactive isotopes opened up the possibility of tagging various constituents of cells and

tissues. Simultaneously, the discovery by Pauling of an electrophoretic abnormality in the hemoglobin of sickle cell disease led to the discovery of all manner of "new" hemoglobins (such as C, D, E, G, H, I, and J) and to an enormous expansion in the knowledge of the "hereditary" hemoglobin disorders and of their racial and geohematological manifestations (fig. 1). It seemed that every road led to the fundamental chemical processes of the cell and its metabolic activities and to the inner mysteries of the disease itself. Morphology, physiology, therapy—all required the chemical approach.

One can distinguish thus three great eras of hematological development in the past century, actually even since 1900: (1) the era of morphology and of descriptive studies, 1856-1926; (2) the era of physiopathology, 1926 to the present; and (3) the era of chemistry, 1945 to the future. Illustrative is what has happened in hereditary spherocytosis (fig. 2). In era 1, there are the descriptions of the disease (acholuric jaundice, familial hemolytic jaundice) and of the abnormal cell involved, i. e., the spherocyte; and there are studies of the hypotonic fragility and the thickness-diameter ratio. In era 2, there are studies of the disturbed physiology: the bile pigment output, the life span of the red blood cell, the mechanism of splenic trapping, and the reasons for the remarkable effects of splenectomy. In era 3, our own, we begin to study the "why" of the spherocyte itself, its chemistry, its carbohydrate enzymatic abnormality, and even methods by which the abnormal cell might conceivably be modified. Similar thoughts hold true for sickle cell anemia (fig. 3).

Hematology in 1956 has thus become an exceedingly diverse and complex field, so much so that to few men is given the ability to encompass all of it. The simple

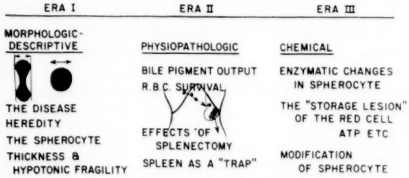

Fig. 2.—Eras of concepts concerning heredity spherocytosis in the last century.

little hematology laboratory of 1920 or thereabouts has blossomed out into a state of complexity. Simultaneously, the expense of hematological investigation has risen almost perpendicularly. One sometimes wonders whether productivity has gone up at a parallel rate. To cover the expanding literature of hematology, many new journals have been founded, three in the past few months. One of them "Thrombosis et Diathesis Haemorrhagica" is the first devoted to a subspecialty of hematology.

Hematology in the Future

We have seen hematology in the past, and we have noted the present status of hematology. What is to be the future? There can of course be no doubt of the ever-increasing expansion of the field and of the division and subdivision of such fields as the coagulation disorders, immunohematology, and the hemoglobin abnormalities, to mention but a few. Soon one man will hardly be able to encompass even one fraction of

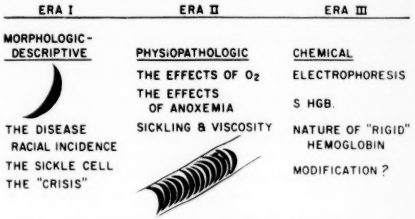

Fig. 3.—Eras of concepts concerning sickle cell disease in the last century.

one of the hematological subspecialties. This is by no means an unmixed blessing, as we note the extreme erudition of the younger group concerning a certain very small field of hematology and their relative ignorance when other fields are discussed.

What can one prophesy further? Certainly the gradual, perhaps the quick, control, as their mechanisms are worked out, of a number of now hopeless or near hopeless conditions. For example, one can with some justification predict that leukemia will be controlled; not necessarily cured, but controlled. The amazing specificity of some of the chemotherapeutic methods, the possibility of a viral etiology for at least some cases of leukemia, and therefore the possible development of methods of prophylaxis as in poliomyelitis—these are optimistic portents. Methods for bone marrow preservation and for bone marrow transfusion will almost certainly be developed. The necessity is there; the tools for preserving marrow are at hand; more work and techniques are all that are required. Bone marrow stimulants, conspicuous nowadays by their lack, will undoubtedly be found.

The chemical and enzymatic defects of the red blood cell in the hemoglobinopathies will almost certainly be discovered and perhaps then methods devised for so modifying them that the red blood cell survival will become normal. For the hemophilias, undoubtedly the deficient materials (such as antihemophilic globulin) will be concentrated and prepared for daily injection like insulin. One can speculate about the possible development of antiantibodies which could conceivably control certain cases of hemolytic anemia, leukopenia, and thrombocytopenia.

It is well to realize that, in all of these developments to come, we must be dependent not only on what we ourselves do in our own laboratories but

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upon the work of our colleagues in other cities, in other lands. No scientist works in a vacuum, and we rely more than we realize upon the work of many individuals, upon our contacts in meetings such as this, and upon the world's medical literature. In the nature of things, science can never be parochial.

This brings us to the last portion of this discourse. One would be remiss at an international gathering of this sort not to mention something of the political problems and their implications. Doctors, particularly hematologists, are of course a highly specialized group, but they work within the framework of society and must therefore enter into it as active participants. Gathered here is a cross section of men and women from various lands, men and women of various religions and political beliefs—a microcosm. In many cases these people have come here despite considerable difficulty, financial for the most part, political in some cases. They have come here as men of good will, intensely interested in gathering as much knowledge as possible and passing on what they themselves know to their colleagues—of whatever land and of whatever political belief. Such has been the custom of scientific groups for centuries. Our delegates have seen that their colleagues of another country, another continent, or another political belief are fundamentally the same sort of people, equally dedicated to their work as physicians, anxious to learn, anxious to teach—in other words, a great fraternity.

This is the most important lesson I myself learned on my recent world tour, part of it behind the so-called Iron Curtain. Face-to-face contacts inevitably lead to the simple but profound conclusion that people are fundamentally the same, with similar aspirations and ideals, whatever their language or their skin color. Such contacts must surely help to reduce the often artificially exaggerated differences between people of one country and another. An international gathering of this sort, and gatherings of other groups of scientists or business men or farmers or even of plain tourists, will surely break down barriers, whether iron or bamboo. This is a very important first step toward world peace and toward doing away with mankind's number one disease—war. As physicians and investigators, we need a steady "climate" of peace so that we can proceed unhindered in our studies and in the ultimate conquest of man's illnesses and man's fears. As hematologists, we must ever work to prevent useless blood loss and to conserve this most precious fluid for an increasingly healthy society.

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HEPATIC-TYPE "FLAPPING TREMOR" OCCURRING IN PATIENTS WITHOUT HEPATIC DISEASE

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and
Naseeb B. Baroody, M.D., Florence, S. C.

The alteration of consciousness and the aberrant behavior of patients with severe hepatic disease in its terminal stages have been known to clinicians for years.[1] However, not until Adams and Foley [2] reported the results of a clinical and pathological study of the neurological changes found in patients dying of cirrhosis and other hepatic diseases was the significance of the abnormalities seen in these patients widely appreciated.

As a result, clinicians now have a new sign commonly called the "liver flap" or "flapping tremor." Adams and Foley [2] describe this as follows:

Clinicians have a new sign commonly called the "liver flap" or "flapping tremor," described as a characteristic type of involuntary movement or "peculiar intermittency of sustained muscle contraction." While primarily a useful sign of impending liver failure it has also been observed in patients with uremia, polycythemia vera, severe malnutrition, and steatorrhea. In addition, the sign has been found in some patients with azotemia without hepatic disease. It is emphasized that this type of tremor although characteristic of, is not solely diagnostic of, impending or existing hepatic failure.

From the Medical College of South Carolina and Roper Hospital (Dr. Smythe) and McLeod's Infirmary (Dr. Baroody). Dr. Smythe is a Markle Scholar and Associate in Medicine at the Medical College of South Carolina.

. . . a characteristic type of involuntary movement. This was most consistently and effectively demonstrated by having the patient hold his arms and hands outstretched with the fingers spread apart. Depending on the severity of the process, as this posture was maintained there appeared at irregular intervals of a fraction of a second to seven seconds, a series of movements consisting usually of lateral deviations of the fingers, flexion-extension of the fingers at the metacarpophalangeal joint, and flexion-extension at the wrist. The movements were rapid and arrhythmic, and one phase . . . was always more rapid than the other. They tended to occur in bursts, at a rate of every second or two.

This "peculiar intermittency of sustained muscle contraction" has emerged as a most useful sign of impending liver failure. However, Adams and Foley,[2] in their original paper, mention that they had observed it in two patients with uremia and in three with polycythemia vera. More recently Cooke [3] has described this sign in patients with severe malnutrition and in three patients with steatorrhea.

A young woman with lupus erythematosus disseminatus and moderate azotemia and a young man with hypertensive cardiovascular renal disease were observed to have gross "flapping tremor" for a period of a few days. Their cases are being reported to reemphasize Adams and Foley's original contention that this type of tremor, although characteristic of, is not diagnostic of, impending or existing hepatic failure.

Case 1.—A 34-year-old Negress was first noted to have a butterfly rash in July, 1953. Aside from chronic pelvic inflammatory disease, mild toxemia during her last pregnancy in 1948, and a doubtful serology, nothing was noted of apparent significance to her later illness during her long attendance at various clinics of the Roper Hospital. A tentative diagnosis of lupus erythematosus was made but not proved, and the patient was later considered to have seborrheic dermatitis. Four months later she developed pneumonia in the lower lobe of the left lung with pleural effusion which necessitated hospital admission. On this admission, albumin, red and white blood cells, and casts were found in the urine. A bone marrow preparation was positive for L. E. cells.

The patient did not improve satisfactorily after discharge, and readmission was necessary seven months later, in June, 1954, for pyoderma. In the interval the patient had developed asthma, and she was hypertensive, with a blood pressure of 180/100 mm. Hg. The urinary sediment was again grossly abnormal. After her discharge, repeated infections of the skin, conjunctivas, and external auditory canal plagued her. She was readmitted to the hospital in November and in December cortisone therapy was started. Her blood pressure was at a level of 170/110 mm. Hg. In the days before admission, she had noted that her rash had become more papular. After an episode of gross hematuria, her temperature was 103 F (39.4 C), and she was admitted with a diagnosis of bilateral pneumonitis. Physical examination revealed an obese moon-faced woman in considerable respiratory distress. There was hyperpigmented papular rash over the bridge of her nose and cheeks. Her temperature was 100.4 F (38 C), pulse rate 120 per minute, respirations 22 per minute, and blood pressure 140/100 mm. Hg. The heart was slightly enlarged and, except for sinus tachycardia, was otherwise not remarkable. Dulness to percussion was found over the left lower lung field, and fine rales and expiratory wheezes were heard at the bases of both lungs. The liver was palpable at the right costal margin and was tender. The area of hepatic dulness was not increased. There was generalized abdominal tenderness. Laboratory data for this case are summarized in the table.

On her fourth hospital day the patient developed acute respiratory distress with severe pleuritic pain on the left side and signs of acute left-ventricular failure. Her temperature was 104.2 F (40.1 C). She began to cough pink sputum in which pneumococci were seen (later cultured) on Gram staining. She was thought to have pneumococcic pneumonia of the lower lobe of the left lung and acute pulmonary edema. She responded to intravenously given lanatoside C and tetracycline. Pleural effusion later appeared on the left and the liquid was aspirated.

After this acute episode the patient improved. On the morning of Nov. 18, or four days after the acute episode and eight days after admission, it was noted that she had developed a spontaneous arrhythmic tremor of her hands. This was accentuated when the arms were extended and involved primarily the fingers and wrists. The flexor phase of the tremor was more rapid than the extensor. The patient was quite alert and was well aware of the jerking, which she could not control. The tremor was much worse in the morning and tended to decline as the day progressed. At the time the tremor was first noted, the patient was receiving prednisone, 25 mg. every six hours; tetracycline, 200 mg. every six hours intramuscularly; sulfisoxazole (Gantrisin), 1 Gm. every six hours by mouth; aminophylline suppositories, 0.5 Gm. every four hours; digitalis, 0.1 Gm. daily; phenobarbital sodium, 30 mg. every six hours; and codeine, 30 mg. every four hours, principally for pain. When the tremor was noted, the prednisone dosage was cut to 15 mg. every six hours and the use of the barbiturate was discontinued.

Laboratory Data for Case 1

Date, 1955	Nov. 12	Nov. 20	Nov. 21	Nov. 28	Dec. 2	Dec. 5
Leukocytes, thousands/cu. mm.	34.5	23.7			9.2	
Hemoglobin, Gm./100 cc.	12.5	11.5			10.5	
Urinary specific gravity	1.012		1.020		1.018	
Urinary albumin	4+		3+		3+	
Leukocytes, high-power field	20-30		50		300	
Erythrocytes, high-power field	1-2		10-15		10-15	
Blood urea nitrogen, mg./100 cc.	18	126	63	29		24
Blood sodium, mEq./liter	140	138	140	135		139
Blood potassium, mEq./liter	4.2	7.5	6.2	5.1		4.6
Carbon dioxide, vol. %	38		40			46
Calcium, mg./100 cc.			8.7			7.5
Phosphorus, mg./100 cc.			10.4			5.4
Total protein, Gm./100 cc.	6.79					
Globulin, Gm./100 cc.	3.66					
Alkaline phosphatase, King-Armstrong units/100 cc.		9.6				
Sulfobromophthalein retention, %			0			
Cephalin-cholesterol flocculation		Negative				
Prothrombin time, %			100			

The next day the tremor was still present, and the day after that it was at its height. On this day the patient had difficulty holding a glass, but she was able to walk, although unsteadily because of weakness. At no time were abnormalities of reflexes or muscle tone noted. An electroencephalogram was not made. Blood-chemistry findings at this time are noteworthy for a blood urea nitrogen level of 126 mg. per 100 cc. (63 mg. the next day), a calcium level of 8.7 mg. per 100 cc., and a phosphorus level of 10.4 mg. per 100 cc. All hepatic-function tests were within normal limits (see table). The liver was not enlarged, and there was minimal tenderness in the right upper quadrant. There was no icterus. Four days after the tremor appeared, it began to decline, never to reappear. The patient is progressing fairly well, without azotemia at present, on therapy with 20 mg. of prednisone a day.

Case 2.—A 33-year-old Negro man was admitted to McLeod's Infirmary, Florence, S. C., on Jan. 4, 1956, complaining of epigastric pain of one week's duration. He had vomited intermittently for two to three days prior to admission and during the same time had noticed the onset of a nonproductive cough. He gave a history of hypertension, which had previously been asymptomatic.

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On physical examination he was found to be a well-developed, well-nourished male, complaining of abdominal pain. His temperature was 98.6 F (37 C), pulse rate 88 per minute, respirations 22 per minute, and blood pressure 260/140 mm. Hg. Examination of the eyes revealed pale fundi with severe arteriovenous nicking and an arteriovenous ratio of 1:4. The chest was symmetrical, and the lungs were clear to percussion and auscultation. The heart was enlarged to the sixth intercostal space at the anterior axillary line. The border of the left side of the heart was percussed 3 cm. lateral to the midclavicular line. The rhythm was normal, and the aortic second sound was louder than the pulmonic second sound. There was a soft blowing systolic murmur at the apex. Examination of the abdomen revealed epigastric tenderness. The liver was not enlarged and the spleen could not be felt. There was no costovertebral tenderness. The examination otherwise showed results within normal limits.

The laboratory data were as follows: erythrocyte count 3,350,000 per cubic millimeter, hemoglobin level 11.5 Gm. per 100 cc. (69%), leukocyte count 13,600 per cubic millimeter, polymorphonuclear leukocytes 71%, lymphocytes 13%, monocytes 4%, and eosinophils 2%; there was slight poikilocytosis. Urinalysis showed a specific gravity of 1.010, a pH of 7.0, albumin 2+, and sugar negative. There were 2 to 3 leukocytes per high-power field, innumerable erythrocytes, pinkish amber color, and no casts. The serologic test for syphilis was negative. The blood urea nitrogen level was 68 mg. per 100 cc., and the serum amylase level was 72 units. Sickle-cell preparation revealed no immediate sickling, 60% sickling in 24 hours, and 100% in 48 hours. An electrocardiogram was interpreted as indicating sinus tachycardia, left-axis deviation, left-ventricular hypertrophy, and coronary insufficiency. A roentgenogram of the chest revealed cardiac enlargement. Diagnoses of hypertensive cardiovascular renal disease with probable chronic glomerulonephritis, azotemia, sicklemia, and gastritis were made.

The patient was given atropine sulfate, 0.6 mg. every four hours; aluminum hydroxide (Amphogel), 8 cc. every eight hours; magnesium sulfate, 4 cc. intramuscularly every six hours for four doses; and phenobarbital, 30 mg. every eight hours. He was put on a low-salt diet and given 0.4 mg. of digitoxin every eight hours for three doses, then 0.1 mg. daily. His urinary output was good. Fluids were given ad libitum. He was then given 40 mg. of pentolinium tartrate every eight hours. By the fourth hospital day, the blood pressure had dropped to 190/90 mm. Hg and the patient complained of syncope on standing, although he seemed generally improved. Pentolinium dosage was reduced to 20 mg. every eight hours. By the seventh day, the blood pressure once again rose to 240/140 mm. Hg and intractable singultus was noted, for which 25 mg. of chlorpromazine was given every three hours, with little benefit. By the eighth hospital day the blood urea nitrogen level had risen to 117 mg. per 100 cc., singultus continued, and the patient was somewhat lethargic. The blood pressure remained elevated, and the pentolinium dosage was increased to 100 mg. every eight hours. On the ninth hospital day, the blood pressure was 236/140 mm. Hg. The specific gravity of the urine on three separate occasions was 1.010. On the 10th hospital day pentolinium dosage was increased to 200 mg. at 8 a. m., 100 mg. at 2 p. m., and 200 mg. at 8 p. m. The following day there was a drop in blood pressure to 180/110 mm. Hg. On this day, it was noted that the patient's lethargy was somewhat increased and that he had a definite "flapping tremor" when the arms were extended. The flexion-extension tremor involved the fingers, wrists and hands, and infrequently the entire arm. He could answer questions in a logical manner, but his speech was slurred and his responses were extremely slow and delayed. If undisturbed for a few minutes he would fall asleep. Neurological examination at this time revealed intact cranial nerve function and normal deep-tendon reflexes. No abnormal reflexes were observed. No electroencephalogram was taken. By the 12th hospital day the blood pressure reached 200/120 mm. Hg and the patient seemed more alert. The tremor was no longer demonstrable. Singultus was noted only at irregular intervals and the patient appeared to be completely clear mentally. The blood urea nitrogen level was 81.6 mg. per 100 cc. the next day, and the total serum bilirubin level was 0.43 mg. per 100 cc. Cephalin flocculation was 2+ in 24 hours and 4+ in 48 hours. This was considered to be consistent with the sicklemia. The patient was alert and cheerful and took food and fluids well. For the next five days, his consciousness varied from alertness to mild lethargy, at which time he would answer questions logically but in a sluggish manner. The tremor was not subsequently demonstrated. The blood urea nitrogen level on the 18th hospital day was 71.6 mg. per 100 cc. The patient remained alert, ambulatory, and asymptomatic, except for slight postural dizziness, until discharge on the 20th hospital day.

On Feb. 22, 1956, the patient was readmitted with recurrence of abdominal pain, nausea, and vomiting. He had discontinued taking digitalis and presented recurrent symptoms of of orthopnea, dyspnea, and edema. On physical examination the blood pressure was 190/130 mm. Hg and there were scattered moist basilar rales in both lungs. The heart was enlarged and the apex was in the sixth intercostal space at the anterior axillary line. The abdomen was soft and flat and there was moderate midepigastric tenderness. The liver was slightly tender and the lower edge was palpated at the right costal margin. There was 2+ pitting edema of both lower extremities, and diagnoses of malignant nephrosclerosis with hypertensive cardiovascular disease and congestive heart failure were made. The blood urea nitrogen level was 130 mg. per 100 cc. and the hemoglobin level had dropped to 5 Gm. per 100 cc. For the next five days his condition was poor. He developed urinary retention and on several occasions catheterization was necessary. Nausea and vomiting continued. On the fifth hospital day he became irrational and confused. He died on the seventh hospital day.

At autopsy, the final anatomic diagnoses were (1) marked generalized arteriosclerosis, (2) marked cardiac hypertrophy (cor bovinum), (3) arteriolar nephrosclerosis, (4) focal myocarditis, (5) acute and chronic pancreatitis, (6) congestion of viscera, and (7) lipoma of the left adrenal gland.

Comment

These are complex cases. It is, however, fair to say that neither patient had clinically apparent hepatic disease and that there was little evidence of hepatic dysfunction. The first patient had lupus erythematosus with findings indicative of renal injury and evidence of lowered resistance to infection. The second had renal failure on the basis of nephrosclerosis. At the time of the episode of "flapping tremor" both patients were markedly azotemic, and it was thought that death from uremia would rapidly ensue in each instance. However, those who observed the tremors in these cases felt that these were not the extensor twitches or spasms or jactitations of uremia but true flexion-extension tremors identical with those seen in patients with hepatic failure. They were not caused by simple loss of muscle strength. It is of interest to note that, in the first patient, after the dosage of prednisone (which had been increased with the idea that it might control the apparently increasing renal damage) was reduced and then omitted, the kidney status improved rapidly. The same sequence with pentolinium tartrate occurred in the second patient. It should also be mentioned that the first patient was having considerable respiratory distress at the time of the occurrence of the tremor. Although arterial oxygen saturation was not measured,

the patient was not clinically cyanotic. Bessman and Evans [4] have noted elevated blood ammonia concentrations in chronic congestive failure.

In the past few years the major investigative effort on the pathogenesis of hepatic coma has been directed at determining the exact role of ammonia and at elucidating the disorder of its metabolism seen in such patients. Although probably not the only factor, retention of ammonia is recognized as being closely related to the clinical picture of hepatic coma.[5] However, the severity of the neurological disturbance has not been found to correlate too closely with peripheral venous levels of blood ammonia.[6] Webster [7] has postulated that the cerebral production, and therefore the ammonia content, of jugular venous blood may be a determining factor. The severity of the neurological disturbance has also been found to correlate most closely with the arterial blood ammonia level.[8] Most of these investigations have been concerned largely with the alteration of consciousness. Whether the tremor is related to the same metabolic derangements as the stupor is not definitely known, but probably it is related. The close resemblance of the tremor to other neuromuscular disorders arising from disease of the basal ganglions and the description of astrocytic abnormalities in this portion of the brain [2] are evidence of a special sensitivity of the cells of this area to the abnormal metabolic processes involved.

Adams,[2] Davidson,[9] and Bessman [8] have observed that persons with uremia demonstrate a typical "flap." Bessman [8] has reported on blood ammonia levels in four persons (part of his comatose control group) with uremia. All levels were within the normal range. It has been pointed out that this is to be expected, since, in part, ammonia levels depend on renal production, and in uremia this source is markedly curtailed.[5] Moreover, since many feel that high blood ammonia levels in persons with cirrhosis are almost totally dependent upon escape of the ammonia in the general circulation via collateral channels bypassing hepatic parenchyma,[10] one would not expect a high ammonia blood level in persons with uremia, without liver disease, and in whom no such collateral circulation exists. No description of ammonia retention in patients with uremia has been found. Therefore, the patients in our study, having intact liver function and absence of an extensive collateral circulation, may be assumed to have had normal ammonia levels, although it cannot be concluded definitely that there was no ammonia retention without actual measurements. This leads to the conclusion that the tremor of hepatic coma may not be due solely to ammonia retention and that the neurological disorder seen in these patients probably had other contributing causes.

Summary

A "flapping tremor" occurred in two patients who had azotemia but not hepatic disease. Both patients recovered from the episodes of renal failure. One patient subsequently died, and at autopsy the liver was found to be essentially normal.

Addendum

The first patient has subsequently died. At autopsy there was no liver disease. The kidneys showed extensive changes consistent with a diagnosis of lupus erythematosus.

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Sudden Deafness.—A study was made of 178 cases of sudden deafness of obscure cause encountered in a five-year period, 1949 to 1953, inclusive. In 89 cases the deafness seemed to be due to a vascular accident. In 56 it seemed to be due to Ménière's disease. In 17 the cause could not be determined. In 15 it was due to miscellaneous causes usually of infectious origin. In one case the deafness was thought to be due to hysteria or malingering. The literature, pathology, etiology, diagnostic factors and other pertinent data were considered in some detail. Because of the absence of specific information as to the underlying pathology, the diagnosis as to etiology has to be somewhat tentative; however, in most of the cases studied, repeated and extensive examinations permitted a statement as to etiology which is considered fairly authoritative.—O. E. Hallberg, M. D., Sudden Deafness of Obscure Origin, *The Laryngoscope*, October, 1956.

SERUM LACTIC DEHYDROGENASE–A DIAGNOSTIC AID IN MYOCARDIAL INFARCTION

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The usefulness of specific enzyme reactions to clinical medicine is becoming increasingly more apparent. Patients suffering destruction of various tissue cells have increased enzymatic activity in their serum. The enzymes normally present within the cells are liberated into the blood stream as cell destruction occurs. The determination of serum lactic dehydrogenase (LDH) as an aid in the diagnosis of acute myocardial infarction has two advantages: first the increased elevation is present for as long as six to eight days after attack; second, the technical procedure is far less complicated than other enzyme tests. LDH determination, not ordinarily necessary in the diagnosis of acute myocardial infarction, is particularly helpful when the electrocardiograph pattern masks the recent changes of an acute infarction.

Abnormally elevated serum enzyme levels resulting from tissue destruction are assuming increasing importance as diagnostic procedures. The discovery that glutamic oxaloacetic transaminase is released from cardiac tissue during myocardial infarction [1] led to a search for other enzymes which might behave similarly. Wróblewski and LaDue [2] noted the presence of lactic dehydrogenase (LDH) in serum and subsequently demonstrated its elevation after acute transmural myocardial infarction. Hill and Levi [3] previously reported finding an elevated level of a serum component in neoplastic disease which they believed to be lactic dehydrogenase. Others [4] have reported LDH elevations in various other disorders.

The present report describes the method of analysis for LDH and presents the findings in 174 hospital patients representing many different pathological conditions.

Method

Methods for the assay of LDH are usually based upon the oxidation or reduction of diphosphopyridine nucleotide (DPN) or reduced diphosphopyridine nucleotide (DPNH). These reactions are coupled with the conversion of lactic acid to pyruvic acid or vice versa. Maximum reduction by LDH occurs when pyruvic acid forms lactic acid. DPNH in this case furnishes the proton required for the reaction and is consequently oxidized to DPN. This is the principle of the procedure used in this study.

The method is essentially that of Wróblewski and LaDue.[2a] It has been modified by dilution of the serum when an appreciable drop in the rate of DPNH oxidation occurs during the period of measurement.

To 2.4 ml. of phosphate buffer (pH 7.4) add 0.1 ml. of serum and 0.1 ml. of DPNH (2.5 mg. per milliliter in water, made basic to pH 9.0 with sodium hydroxide). Allow to stand 20 minutes, then add 0.1 ml. of sodium pyruvate (2.5 mg. per milliliter). The optical density of the solution is then read every 15 seconds for 5 minutes at 340 mμ in a Beckman DU spectrophotometer. If the optical density decreases at an accelerating rate for each time interval, dilute an aliquot of the original serum with phosphate buffer and repeat the procedure using the original amounts of all constituents. Appropriate dilutions are indicated by the first minute readings: 1:3 if over 1,000, 1:4 if over 1,500, or 1:5 if over 2,000 units. Further dilution may be necessary if the LDH activity is extremely high. The rate of decrease of optical density is taken as a measure of LDH activity expressed as units per milliliter of serum per minute. One unit equals a decrease in optical density of 0.001 per minute per milliliter under the above conditions. Any dilution must also be considered in the calculation of the final value.

The 20-minute time interval after addition of the DPNH is required to permit the reduction of alpha-keto and alpha, gamma-diketo acids initially present in the serum. This reaction stops when the keto and diketo acids are enzymatically reduced to lactate by the added DPNH.

No specific dilution factor can be given since this will depend upon the LDH activity of the serum and the assay of the DPNH preparation used, for the latter may vary from one lot to another. Insufficient quantities of DPNH will be indicated by a decreasing rate of reaction. Serum dilution decreases the LDH activity to a known degree, thus making the amount of DPNH adequate for the reaction. If the rate of reaction is not periodically followed, an inadequate DPNH activity will not be apparent. Methods which measure optical density initially and after a specified time interval will give lower values than those obtained by the technique described above, especially if LDH activity is very high.

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Hemolysis must be carefully avoided since the LDH activity of whole blood hemolysates is approximately 100 times that of serum.[2a] Any perceptible hemolysis will give falsely elevated results. The serum may be stored at 4 C (40 F) for 3 days or frozen for 10 days.[3] Slightly lipemic or icteric serum may be used for the determination.[3]

The serum LDH activity in 40 normal adults selected from hospital personnel (20 males and 20 females, aged 20 to 64) varied from 165 to 332 units, with a mean of 247 units. Standard deviation for this series was 33 units. The mean ±2 standard deviation units (sigma) should include 95% of the values in the series (95% confidence limits of a normal distribution). Only one subject was found to have a serum LDH level above this (332 units). Therefore the normal range of LDH activity is below 313 units when determined by the above procedure.

Summary of Conditions Studied and Elevated LDH Levels

Disease	No. of Patients	LDH Elevations: Above Normal	LDH Elevations: Above 500 Units
Heart disease	**94**		
Angina pectoris	13	0	0
Myocardial infarction	50	50	44
Coronary insufficiency	15	5	3
Congestive failure	12	4	3
Pericarditis			
Tuberculous	2	2	2
Idiopathic	2	1	1
Liver disease	12		
Viral hepatitis	6	5	4
Laennec's cirrhosis	5	1	1
Traumatic necrosis	1	1	1
Pulmonary disease	**8**		
Pneumonia, lobar	4	2	0
Infarction	2	1	0
Lung abscess	1	0	0
Necrosis	1	0	0
Cerebral vascular accidents	11	11	3
Diabetes mellitus	7	3	0
Malignant disease	13		
Lymphomas	5	4	1
Multiple myeloma	2	1	1
Metastatic carcinoma	4	4	2
Sarcoma	1	0	0
Myelogenous leukemia	1	0	0
Hematological disease	5		
Sickle cell anemia	3	3	3
Hemolytic crisis	1	1	1
Infectious mononucleosis	1	1	1
Miscellaneous diseases	19	7	0
Pregnancy	5	1	0
Totals	174	108	71

Clinical Studies

Clinical material consisted of 174 hospitalized patients, 94 with organic heart disease. Seventy-eight patients were suffering from coronary artery disease. In addition to frequent clinical observation, cardiac patients were studied by serial determinations of white blood cell count (WBC), erythrocyte sedimentation rate (ESR) by the Westergren method, 12-lead electrocardiogram (ECG), and LDH levels. Many other conditions were also studied, especially those considered in the differential diagnosis of acute myocardial infarction.

A tabulation of the conditions studied and the number with LDH levels above normal and above 500 units is shown in the table. Patients are grouped according to clinical diagnosis at the time of leaving the hospital.

Angina.—Of the 13 patients with angina pectoris, 5 were not suspected of having myocardial infarction. All five had essentially normal WBC, ESR, and ECG tests that in no way suggested or masked myocardial infarction. The LDH levels were normal in all. These results compare favorably with those of others who have demonstrated normal serum enzyme levels in the absence of myocardial tissue destruction.

Myocardial Infarction.—In 44 patients (37 males and 7 females aged 43 to 83) the diagnosis of acute myocardial infarction was definitely established by clinical, electrocardiographic, and/or postmortem pathological studies. The infarction was considered transmural in all. Six additional patients in whom the diagnosis of infarction was in doubt were considered separately as infarction suspects.

LDH levels were elevated in all 44 patients and above 500 units in 39 patients. The lesser degrees of elevation occurred under the following circumstances: Two patients whose single LDH levels of 320 and 380 units were determined 12 and 18 hours after onset of the attack died shortly thereafter. One patient, studied only on the first day, had an LDH level of 340 units. Definite onset time could not be established in another patient whose top level was 400 units. An elderly woman who suffered cerebral thrombosis at the time of coronary thrombosis had a maximum value of 495 units on the sixth day.

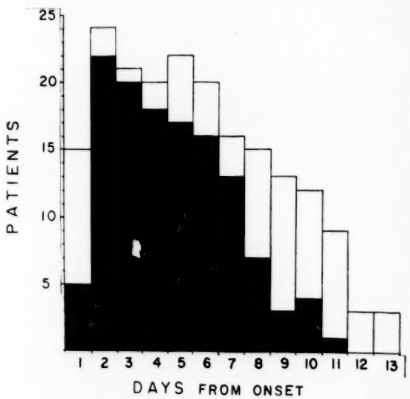

Fig. 1.—Significant elevations of LDH levels after acute transmural myocardial infarction. Total height of bar equals number of determinations. Shaded area denotes number of determinations above 500 LDH units.

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The time of onset of the attack leading to myocardial infarction was established in 38 patients. This was based primarily on the appearance of characteristic retrosternal pain, collapse, shock, or various arrhythmias. Such timing was not possible in six patients.

Serial determinations of LDH activity were obtained daily in many patients. Rise in LDH level in response to myocardial infarction began on the first day. Maximum levels were usually reached on the 2nd or 3rd day and slowly declined to normal by the 6th to 11th day. This trend is illustrated in figure 1, which utilizes LDH determinations in patients with definitely established onset.

A delay in return of LDH level to normal, or a secondary rise, implied extension of the infarction and often a much poorer prognosis. The LDH level of patient F. C. shown in figure 2 is illustrative. This woman died after 10 consecutive days of LDH elevation above 900 units. Extreme elevations (above 2,000 units) did not prove prognostically significant. Three patients with levels of 4,000, 2,950, and 2,960 units died, but two others with levels of 2,250 and 2,650 units had uncomplicated clinical courses. No correlation was attempted between the size of infarct at autopsy and the degree of LDH elevation. Fifteen patients died during the period of study for a mortality rate of 34%. Four hearts were studied at autopsy and all showed definite evidence of acute transmural myocardial infarction.

Infarction Suspects.—In 29 patients (19 males, 10 females, aged 39 to 74) recent myocardial infarction was suspected but not definitely established by initial studies. Thirteen of these had suffered previous myocardial infarction from two weeks to five years earlier. After careful and intensive study these 29 patients were finally given diagnoses as follows: angina pectoris, 8; coronary insufficiency, 15; and myocardial infarction, 6. There were no deaths during the period of study. All of the eight patients with angina had normal LDH levels.

Of the 15 patients with coronary insufficiency 10 had had a previous myocardial infarction and their electrocardiograms showed patterns of old myocardial infarctions that could have masked recent changes. In 7 of these 10 the LDH levels were normal while in the remaining 3 they were maximally elevated to levels of 545, 555, and 595 units. Actual myocardial necrosis probably occurred in these three patients.

In the remaining five without previous infarction, the electrocardiograms showed patterns of ischemia in all. Three of these had normal LDH levels but in the other two the levels were elevated to slightly over 400 units, probably due to small areas of subendocardial necrosis.

In the last group of six patients conclusive electrocardiographic evidence of infarction was lacking. Masking patterns of bundle-branch block and old infarction were present in five while in the sixth minor changes in lead AVL suggested lateral infarction. LDH levels in this group were slightly to moderately elevated (410 to 700 units). The lesser elevations (410 and 460 units) were found in the two patients with bundle-branch block. LDH levels in the three patients with old infarction were 615, 700, and 540 units. The man with the lateral infarction had his maximum LDH elevation (500 units) 36 hours after onset of pain. In this group, as in the previous ones, LDH elevations seemed to correlate with the presence of necrotic myocardial tissue.

Congestive Failure.—Of 12 patients admitted primarily for treatment of congestive heart failure, 4 had elevated LDH levels and 3 of these were above 600 units. The LDH level was 605 units in a woman with left bundle-branch block due to arteriosclerotic heart disease. A man with rheumatic heart disease and atrial fibrillation had an LDH level of 390 units. His ECG also showed nonspecific myocardial damage. Another man with rheumatic heart disease and atrial fibrillation had an LDH level of 775 units and an ECG which showed subendocardial ischemia. He died while in the hospital, but there was no autopsy. The fourth elevation occurred in a man with secondary polycythemia due to decompensated arteriosclerotic heart disease. His LDH level was 630 units on the day after admission and 340 units two days later. Two electrocardiograms showed severe diffuse myocardial damage and changes suggestive of lateral infarction. LDH elevation in these four patients may have been due to actual myocardial necrosis but final pathological proof was not available.

Pericarditis.—The diagnosis of pericarditis was established by clinical observation and electrocardiographic changes in four patients. In two the disease was felt to be of tuberculous origin, while in the other two no definite etiology could be proved. LDH levels were elevated (530 and 505 units) in the two patients with tuberculous pericarditis. Pericardicentesis was performed on both these patients and LDH levels were determined on the pericardial fluid. The LDH levels (530 and 570 units) approximated those of serum.

One patient with idiopathic pericarditis had consistently normal LDH levels while the other patient showed a transient elevation. LDH levels in the latter varied from 440 units when first studied to a maximum level of 640 units five days later, at the height of clinical disease. Fifteen days later the level had returned to normal.

The LDH activity of normal pericardial fluid has never been recorded, but it seems valid to assume that it would approximate that of serum. The most likely explanation for the increased LDH activity would be destruction of cells in the epicardial layer of the myocardium. Such destruction probably took place in the three patients with elevated LDH levels.

Liver Disease.—Twelve patients with primary liver disease were studied. Of six patients with viral hepatitis the LDH level was elevated in four studied during the acute stage. The highest level was 1,370

units, but most values were between 400 and 600 units. As clinical improvement took place, LDH levels gradually returned to normal. A woman studied approximately seven weeks after a mild attack of infectious hepatitis had a normal LDH level. Another woman who had had an acute attack several months previously and still showed active liver disease had an LDH level of 435 units.

Of five patients with cirrhosis four had normal LDH levels. The fifth had an initial LDH level of 610 units which fell to 425 units in a period of 18 days. The final patient was a window washer who had fractured his liver as the result of a fall. The LDH level was 850 units one week after a portion of the liver had been resected and while there was still evidence of active liver necrosis. LDH determinations seemed of little help in evaluating liver disease because elevations were usually not marked and significant changes took place too slowly. Enzyme determinations other than LDH appear to be more useful in hepatic disease.

Pulmonary Disease.—Eight patients with primary pulmonary disease presented normal or only slightly elevated LDH levels. Of four patients with lobar pneumonia, two had normal values and two others had maximum levels of 380 and 360 units. A man with multiple lung abscesses had consistently normal LDH levels. A woman who had necrosis of the left lung complicating a severe pneumococcic septicemia had a normal LDH level the day prior to total pneumonectomy. Of two patients with pulmonary infarction complicating pulmonary embolism, one had a slightly elevated LDH level (350 units) and the other had consistently normal values. From this limited experience it appears that significant elevation of LDH levels does not occur in pulmonary disease.

Cerebral Vascular Accidents.—Eleven patients with cerebral vascular accidents secondary to hemorrhage, thrombosis, or embolism had elevated LDH levels. The elevation in most cases was slight (350-450), but three patients had levels as high as 700 units and one of these reached 1,060 units. Myocardial infarction was ruled out in all these patients. Significant elevation of LDH levels in these patients was probably related to actual destruction of brain tissue.

Diabetes Mellitus.—In patients with diabetes mellitus LDH elevation appeared to be associated with the presence of ketosis. Four of seven diabetics had normal LDH levels. Two of these four had areas of gangrene on their feet. The conditions of three patients with elevated LDH levels were all poorly controlled, and one patient had ketosis at the time of study. LDH levels were only slightly elevated (410, 360, and 445 units) in these three patients.

Malignant Disease.—Several malignant diseases were associated with elevated LDH levels. The degree of elevation appeared related to the extent of spread of the malignant process. In this group of 13 patients there were 5 with lymphomas. Three of these had Hodgkin's disease and in two the disease was widespread. LDH levels in these two patients were elevated (435 and 475 units). The third patient, who had Hodgkin's disease limited to the mediastinum, had a normal LDH level. Another patient had giant follicular hyperplasia and an LDH level of 355 units. The last of the group had widespread lymphosarcoma and shortly before death had an LDH level of 850 units.

A woman with far-advanced multiple myeloma had an elevated LDH level (530 units), while another woman with the same disease in its asymptomatic stage had a normal LDH level. All four patients with carcinoma with known metastases had elevated LDH levels (380 to 1,320 units). The highest level was found in a patient whose liver was almost entirely replaced by metastatic tumor. Single cases of fibrosarcoma of the arm and subacute myelogenous leukemia were associated with normal LDH levels.

Hematological Disease.—Five patients with hematological disorders all had elevated LDH levels. Included were three patients with sickle cell anemia in whom LDH levels were 600 to 1,050 units. A woman in an acute hemolytic crisis had an LDH level of 1,610 units at the peak of her illness. With clinical improvement, the level fell to 750 units two weeks later. Elevation of LDH levels in these four cases appears related to the hemolysis which was present. A fifth patient with infectious mononucleosis at the height of his illness had an LDH level of 650 units which fell to 495 units five days later. LDH elevation in this male student was probably related to the hepatitis which was present.

Miscellaneous Conditions.—LDH levels were determined in several other conditions with the following results: Of two patients with acute thrombophlebitis of large leg veins, one had a slightly elevated (350 units) and the other a normal LDH level. Of four patients with rheumatoid arthritis, three had normal LDH levels and one had a slightly elevated level (435 units). One patient with ulcerative colitis had a slightly elevated LDH level (370 units) and another patient a normal one. Two patients with uremia secondary to chronic pyelonephritis had levels of 240 and 325 units.

Slight elevations of LDH levels were noted in single cases of fractured tibia (330 units), third-degree burns (435 units), and disseminated lupus erythematosus (330 units). Normal LDH levels were observed in one case of each of the following conditions: hypothyroidism, acute cholecystitis, perforated gastric ulcer, acute diverticulitis, regional enteritis, and Gaucher's disease.

Of five pregnant women four had normal LDH values and in the other the level was minimally elevated (350 units). This latter finding is in disagreement with the results of others,[3] who report LDH elevation in 70% of pregnant women.

Comment

Recent developments in clinical research[5] have established the presence of increased levels of enzymatic activity in the serum of patients suffering

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destruction of various tissue cells. The enzymes normally present within the cells are liberated into the blood stream as cell destruction occurs. The degree of elevation of the particular enzyme under study depends on three factors: (1) the concentration of the enzyme within the cell; (2) the amount of tissue or the number of cells actually destroyed; and (3) the accessibility of the products of destruction to the systemic circulation where the measurement is actually made. These increased levels persist for varying periods after the destruction takes place, depending upon which tissue and which enzyme is involved. Although the enzyme determinations currently being employed reflect nonspecifically the response to destruction of several different tissue cells containing the same enzymes, such determinations yield useful information in many clinical situations. Probably the widest application of this principle to date has been the utilization of glutamic oxaloacetic transaminase as an adjunct in the diagnosis of acute myocardial infarction.[6] Other enzymes (hexose isomerase, lactic dehydrogenase, malic dehydrogenase, and aldolase) have also been used for this purpose.[4b] Glutamic oxaloacetic transaminase,[5e] glutamic pyruvic transaminase,[5f] and aldolase [7] have all been employed by various investigators in studying liver disease. The increasing usefulness of the application of these specific enzyme reactions to clinical medicine is becoming increasingly more apparent.

The results reported here demonstrate the value of LDH determinations as an aid in the diagnosis of acute myocardial infarction. To justify the use of this test there should be certain advantages over those methods currently more widely employed for the same purpose. We feel that such advantages do exist and that the most important one is the prolonged elevation that occurs after mycardial infarction. In a significant number this elevation will be present for as long as six to eight days after attack. This is distinctly helpful in those patients with less severe attacks of myocardial infarction who present themselves several days after the initial attack of pain. Another advantage is the less complicated technical procedure. The method is technically easier, requires fewer reagents, and less frequent determinations are necessary than with the transaminase test. The modified procedure herein described gives accurate values at any level of LDH activity.

Determinations of LDH, although confirmatory, are not ordinarily necessary in the diagnosis of acute myocardial infarction. However, there are situations in which they are distinctly helpful, particularly when the electrocardiographic pattern masks the recent changes of an acute infarction. This occurs not infrequently when bundle-branch block has developed and when patients have had previous myocardial infarction.

In following the course of a patient with recent infarction, a secondary rise in LDH level may indicate extension of the infarct when there are no additional changes electrocardiographically. Another situation in which LDH determinations may prove helpful is in patients with electrocardiograms that present prominent ST interval and T-wave changes without significant Q waves. Although such changes may simply reflect myocardial ischemia, they may also indicate actual necrosis, in either the subepicardial or the subendocardial layers of the myocardium. Under these circumstances an elevated LDH level would indicate actual tissue destruction rather than the less serious ischemia. The extent of LDH elevation in these situations however is usually less than that found with acute transmural myocardial infarction. The significant elevation in our series of patients with transmural infarction was a level above 500 units, which occurred in 39 of 44 patients (88.6%).

The determination of LDH levels may also be useful in the differential diagnosis of acute pain in the chest or upper part of the abdomen. Many acute conditions to be differentiated from acute myocardial infarction

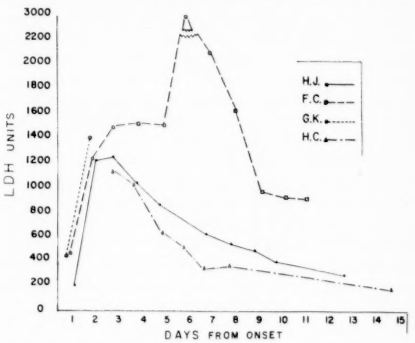

Fig. 2.—Characteristic responses of serum LDH levels after acute transmural myocardial infarction.

have normal LDH levels, e. g., acute cholecystitis, perforated peptic ulcer, pneumonia, pulmonary embolism, and pulmonary infarction. It is admitted that several other diseases (see table) may cause elevation of LDH levels, but these are generally not confused with acute myocardial infarction. The one exception is when coronary thrombosis with resultant myocardial infarction produces a shock-like state that leads to cerebral thrombosis. Both conditions produce significant degrees of LDH elevation, but in the latter condition it is usually less marked. Such a sequence of events occurred in one of our patients.

The various patterns of response reflected by serial LDH determinations are shown in figure 2. The usual response of rise and fall in an uncomplicated case is demonstrated by patient H. J. The prompt rise followed by death on the second day is shown in patient G. K. A stormy course terminating in death on the

11th hospital day is reflected in the determinations on patient F. C. Patient H. C., whose first LDH level was determined on the third day, showed the gradual decline that accompanies a very uneventful clinical recovery.

Other investigators [8] have reported elevated LDH levels in many clinical disorders in addition to myocardial infarction, such as hepatocellular necrosis, metastatic carcinoma, diabetic acidosis, leukemia, megaloblastic and sickle cell anemia, thrombocytopenia, malignant lymphoma, infectious mononucleosis, cerebral infarction and/or hemorrhage, and rheumatoid arthritis. In our studies elevations were also found in most of these conditions, with the exception of rheumatoid arthritis. We found in addition that the LDH level is elevated in acute hemolytic crisis.

These same authors [9] found many conditions associated with normal LDH levels. Included were acute and chronic infectious diseases, pulmonary infarction, localized neoplastic disease, diabetes, peptic ulcer, pancreatitis, cholecystitis, chronic nephritis and uremia, cirrhosis, fractures, myxedema, hyperthyroidism, and arterial thrombosis with gangrene of the leg. This was also true after minor surgery. Patients with heart disease without myocardial infarction usually had normal LDH levels. Our finding of essentially normal LDH levels in pregnant women is in disagreement with others.[3]

Wróblewski [2b] presented two patients in congestive failure with elevated LDH levels but without additional evidence of myocardial infarction. In our group of patients with congestive failure there were four with elevated LDH levels. It was our impression that actual infarction may have been present, but we had no pathological material to support this belief. Further investigation is required to settle this issue.

Although less attention has been focused on the value of LDH levels in other conditions, limited application has been attempted in the field of malignancy.[10] The only conclusion our material permits is the generalization that the degree of LDH elevation in malignant disease appears related to the extent of metastases.

At present it appears that LDH determinations are most useful in the diagnosis of coronary artery disease. In suspected myocardial infarction the serum LDH levels may make possible the diagnosis when all other methods have failed.

This determination is especially useful when the electrocardiographic pattern is masked or when complications occur after myocardial infarction. It often helps to distinguish between ischemia and actual infarction and to differentiate conditions sometimes confused with myocardial infarction. The determination of LDH levels should therefore become a useful laboratory adjunct in the diagnosis of coronary artery disease.

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Summary

A modified method has been described for the determination of serum lactic dehydrogenase (LDH) activity. Elevations of serum LDH were found in myocardial infarction, hepatocellular necrosis, metastatic carcinoma, diabetic ketosis, sickle cell anemia, malignant lymphoma, infectious mononucleosis, and cerebral infarction. The response of LDH levels to myocardial infarction has been described.

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9. Footnotes 2*b*, 3, and 4*a*.

10. Footnotes 3 and 4*d* and *e*.

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CLINICAL NOTES

POSTOPERATIVE ACUTE ADRENAL CORTICAL INSUFFICIENCY

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and
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Until recently, it was common practice in the management of severe postoperative shock for surgeons to use adrenal cortical extracts in the hope that a lack of these substances might be an etiological or contributing factor in the production of shock.[1] A combination of two factors has been responsible for the common failure of such an approach: first, the relative rarity of adrenal cortical insufficiency in the etiology of shock, and, second, administration of inadequate doses of hormones. Knowledge of the physiology of adrenal insufficiency gained during the last five years has made it possible to base corticosteroid therapy on a firmer foundation.[2] Also, the concept of stress stemming from the extensive work of Selye [3] has helped to reveal the importance of the adrenal cortex in the body's response to a host of stressful situations, including major or minor surgery. Much has been learned from the study of patients with adrenal cortical hypofunction (Addison's disease) and patients who have undergone bilateral adrenalectomy.[2b] Modern replacement therapy allows one to operate on such patients with relative safety.[4] Now that it is possible to treat the patient with adrenal cortical insufficiency successfully, it becomes urgent to recognize the clinical condition when it exists.

We have encountered five cases of postoperative shock in which the diagnosis of adrenal insufficiency seems justified. There was no clinical reason to suspect a deficiency of adrenal function preoperatively in any one of these five cases. One of these is presented in detail to illustrate the problem of recognition and treatment.

Report of a Case

A 65-year-old woman was admitted to Huggins Hospital on Oct. 2, 1955, with a history of pain (heavy discomfort) in the right upper abdominal quadrant, penetrating to the right costovertebral angle posteriorly, and accompanied by nausea and vomiting (no hematemesis) of five days' duration. No other symptoms were elicited referable to cardiac or gallbladder disease. Urinary symptoms were denied. The patient's appetite was good, and there was no recent weight loss. The history revealed that the patient had been treated for laryngeal tuberculosis 35 years prior to admission and had thereafter apparently recovered. She had weakness of the back muscles of many years' duration, probably related to an early childhood injury.

Physical examination revealed a woman of small stature. The temperature and pulse and respiratory rates were normal. A movable, nontender, 8-by-12-cm. mass was felt in the right upper abdominal quadrant, and it extended into the right lower quadrant. Other physical findings were limited to the back muscles, which showed organic weakness, but posture was fairly good.

Laboratory determinations showed that the values for hemoglobin, hematocrit, white blood cells, nonprotein nitrogen, blood sugar and amylase, urinary diastase, icteric index, and the Van den Bergh reaction were all within normal limits. Urinary specific gravity was low. Chest x-ray films revealed multiple, tiny, old foci of calcifications at the apex of the left lung, with no evidence of tuberculous activity. Indirect laryngoscopy showed paresis of the left vocal cord and deformity of the larynx consistent with old tuberculosis.

Cholecystography revealed normal filling of the gallbladder and demonstrated a congenital constriction at the junction of the distal and middle thirds of the fundus. An intravenous pyelogram outlined a large tumor mass, at the lower pole of the right kidney, that contained no dye. The left kidney shadow was normal. Cystoscopy with the patient under spinal anesthesia was normal. Retrograde pyelography demonstrated a right ureteral obstruction interpreted as secondary to old tuberculosis. The postcystoscopy course was uneventful.

As part of the patient's preparation for surgery, aminosalicylic acid (PAS) and streptomycin were given to prevent tuberculous reactivation. At operation on Oct. 7, 1955, a large cystic tumor mass replacing the right kidney was mobilized and removed with minimal blood loss. Spinal anesthesia was used. Exploration of the abdomen revealed no disease and confirmed the presence of the congenital constriction of the gallbladder which had been seen on x-ray films. Pathological examination was reported as showing pyelonephrosis, hydronephrosis, and chronic ureteritis.

From the onset of operation there was a tendency toward hypotension and tachycardia; otherwise the patient's condition was good. Blood pressure was maintained by blood-loss replacement and the administration of phenylephrine (Neo-Synephrine) hydrochloride. In the immediate postoperative period, the patient's temperature and pulse rate rose sharply and hypotension became severe, despite adequate blood, fluid, and electrolyte therapy, as shown in figures 1 and 2.

On the first postoperative day unexplained progressive hypotension persisted even with the administration of concentrated arterenol solution. The patient's appearance and color were excellent. She was rational and alert and had no pain or blood loss. Urine output was excellent. Digitalis and oxygen were given for their possible supportive value to the heart, although there was no cyanosis present.

By the third postoperative day, hypotension was severe and the blood pressure was labile. The patient was somewhat confused and had intermittent coldness of the extremities. There was hemoconcentration and marked increase in blood

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Read before the general session, seventh annual combined meeting, New Hampshire and Vermont State Medical Societies, Portsmouth, N. H., Oct. 8, 1956.

viscosity. Arterenol was given continuously, but it was ineffective. An electrocardiogram showed evidence of myocardial ischemia.

The clinical picture suggested adrenal cortical insufficiency, and a total of 250 mg. of hydrocortisone was given intravenously on the third postoperative day. A few minutes after the first dose of 100 mg. of hydrocortisone the blood pressure rose sharply and then gradually stabilized. Subsequently there was rapid improvement in the patient's condition.

On the fourth postoperative day a total of 200 mg. of hydrocortisone was administered intravenously. The patient's blood pressure continued to approach normal. No arterenol was required. The pulse rate, temperature, and hemoconcentration declined. By the 11th postoperative day the patient was fully ambulatory, and the wound was healing well. She went home on the 14th postoperative day.

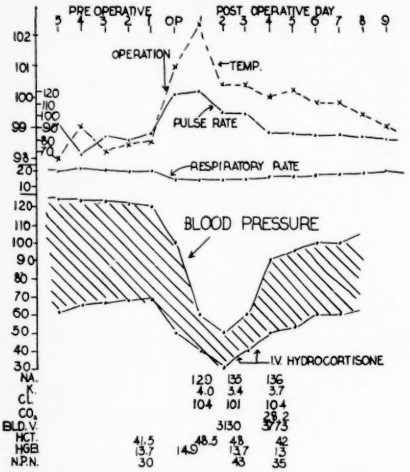

Fig. 1.—Chart showing rise in patient's temperature and pulse rate and lowering of blood pressure during postoperative period, with subsequent rise in blood pressure after intravenous administration of hydrocortisone. At bottom of chart are given values of such blood constituents as sodium, potassium, chloride, and nonprotein nitrogen, as well as the blood volume (in milliliters), carbon dioxide–combining power (in volumes per cent), hemoglobin level (in grams per 100 ml.), and hematocrit reading (in percentage).

Four other cases have been seen at this hospital, of similar type although less dramatic in detail. In each the problem was one of severe hypotension, unexplained by any of the ordinary causes of shock and unresponsive to the usually effective therapeutic measures. Sodium loss specifically was not a cause in any one of the cases.

Comment

A review of case data at the Memorial Center for Cancer and Allied Diseases, New York, indicated that approximately 1 out of every 300 patients subjected to surgery exhibited some form of adrenal cortical insufficiency. The effect of preoperative medication, anesthetization, and operation on the development of postoperative adrenal insufficiency has been suggested by the studies of Schwartz and co-workers [4] on patients with adrenal cortical hypofunction. It appeared that no one drug or method of administering an anesthetic was without harmful effect. Complications occurred proportionately and as frequently with each of the ordinary medicaments and anesthetic agents used. It was also noted that evidence of adrenal cortical insufficiency might develop during any type of operation, including minor procedures. Schwartz and his co-authors recommended that premedication be minimal in dosage. They commented that agents which may produce significant hypotension, such as spinal anesthesia, tribromoethanol (Avertin), and deep inhalation anesthesia, are inadvisable and warned that an alert watch must be kept to avoid hemorrhage and excessive trauma.

A history of prolonged reaction time from anesthesia or the appearance of marked hypotension during previous operations should arouse suspicions of inadequate function of the adrenal cortex. Decreased tolerance to stress is found more frequently in the older age group and in the debilitated patent who has had repeated operative procedures.[5] Also, there is a need for increased cortisone therapy during any form of stress, including surgery in patients with adrenal cortical hypofunction and those who have undergone adrenalectomy, and in those patients who are receiving or who have received cortisone for other condition.[6]

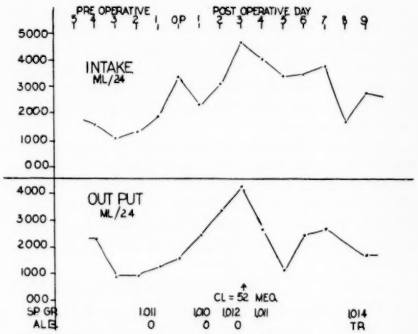

Fig. 2.—Chart showing volume of fluid intake and output (in milliliters per 24 hours) of patient with acute adrenal cortical insufficiency. Under output there are also given such urinary findings as specific gravity amounts albumin. Red blood cell casts were present in the urine on the first, third, and eighth days after operation.

Previous adrenal disease, such as infection (especially meningococcemia or staphylococcemia and tuberculosis), neoplasm, or idiopathic atrophy may result in latent chronic adrenal cortical insufficiency, with the development of adrenal crisis during stressful situations. Secondary adrenal cortical insufficiency as a result of pituitary hypofunction is almost invariably as-

sociated with other anterior pituitary hormone deficiencies and is more commonly recognized prior to surgery.

Persistent hypotension during surgery or in the immediate postoperative period is the most significant sign of the development of adrenal cortical insufficiency.[7] The picture is that of severe vascular collapse, with a failure to respond to adequate blood, fluid, and electrolyte therapy and vasoconstrictor agents. The prompt favorable response to intravenously administered hydrocortisone suggests that the basic physiological disturbance is a deficiency of adrenal cortical secretion. The degree of azotemia, hemoconcentration, and reduced blood volume[8] have been used as indexes of the severity of adrenal cortical insufficiency in adrenalectomized animals and may be similarly useful in man.

It now appears that the intravenous administration of corticotropin (ACTH), with the determination of the levels of 17-hydroxycorticosteroids and 17-ketosteriods in blood or urine, provides the most accurate means of quantitating adrenal cortical response to pituitary stimulation.[9] It has been estimated that the output of hydrocortisone by the adrenal cortex during the stress of surgery and anesthetization normally is approximately 50 to 100 mg. the first day, gradually decreasing to the normal output of 25 to 30 mg. in about five to seven days.[10]

Recently, Perlmutter [11] has proposed a rapid test for adrenal cortical insufficiency useful in the postoperative shock state. As a result of the intensive postoperative adrenal cortical activity, the renal tubules normally absorb most of the sodium from the glomerular filtrate, thus causing a marked decrease in urinary sodium concentration. When adrenal cortical or renal tubular insufficiency is present, sodium output remains relatively high and serum sodium is decreased. The failure of an increased ratio between urine uric acid and creatinine in the first 24 postoperative hours has also been used as evidence of adrenal cortical insufficiency.[12]

Patients operated on for various diseases with an uneventful postoperative course have a maximal decrease in circulating eosinophils on the first and second postoperative days, followed by an increase surpassing the initial level up to the seventh postoperative day. Older patients show a more pronounced eosinophil depression and a delayed eosinophil recovery.[13] The eosinophil response to epinephrine is without much value as a measure of adrenal cortical activity, since the administration of adequate doses of epinephrine has been shown to produce eosinopenia even in the absence of adrenal cortical tissue.

Lipsett and Pearson [14] have recently emphasized that the clinical situation of adrenal crisis is a synthesis of two distinct syndromes, that of sodium loss and that of deficiency of adrenal hydrocortisone. Therapeutically, it is important to distinguish between sodium depletion, deficiency of 17-hydroxycorticosteroids, and a combination of the two.

The mechanism of the effective action of hydrocortisone therapy in subclinical adrenal insufficiency is unknown. It appears that the capacity of cortisone to increase arterial pressure is accentuated in the presence of renal damage and states of adrenal insufficiency. The administration of cortisone alone has been demonstrated to be capable of correcting peripheral vascular failure encountered in acute adrenal insufficiency.[15] Cortisone probably increases capillary resistence [16] and may be necessary to maintain the tone of the terminal vascular bed. In addition, adrenal cortical extracts have been shown to potentiate the action of vasoconstrictors on blood vessels.[17] It may be, therefore, that cortisone has a potentiating effect on vasoconstrictor agents as well as a direct action on peripheral blood vessels.

Effective management depends on recognition of the problem of adrenal cortisone insufficiency. A preoperative test of adrenal response to stress should be made in patients who have exhibited previous surgical hypotension or prolonged reaction time to anesthetization; this test should also be made in the elderly debilitated patient and in those who have had repeated operations. Patients who have received cortisone in the past or who are receiving cortisone currently must be managed with a well-planned preoperative and postoperative regimen of increased cortisone therapy to support them through the period of increased stress.

The cornerstone of treatment is the administration of adequate amounts of cortisone or hydrocortisone. The assumption is never warranted that the clinical syndrome is due solely to salt loss.[14] In addition to adequate therapy with blood, fluids, and electrolytes, intravenously given hydrocortisone results in a dramatic rise and stabilization of the blood pressure and marked improvement of the patient's condition. The administration of hydrocortisone intravenously should be such as to maintain a high level of circulating hormone for several days, followed by a gradual reduction to maintenance levels.

Two possible dangers must be considered when cortisone or hydrocortisone is used for short-term, intensive therapy. Since cortisone and hydrocortisone increase the excitability of the central nervous system, epileptic seizures or psychotic reactions may be precipitated in susceptible patients. Another possible danger is that of excessive sodium retention and the development of edema produced by a high sodium intake during the intravenous administration of hydrocortisone.[10]

Summary

Acute adrenal cortical insufficiency may be an important factor in postoperative shock which does not respond to the usual measures of adequate blood, fluids, electrolytes, and vasopressor agents. Persistent hypotension during surgery or in the immediate postoperative period is the most significant sign of the development of adrenal cortical insufficiency. Effective management depends upon the recognition of this clinical condition and its favorable response to hydrocortisone therapy.

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V 16
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NONABSORBABLE WATER-SOLUBLE CONTRAST MEDIUMS

THEIR USE IN DIAGNOSIS OF INTESTINAL OBSTRUCTION

Bernard S. Epstein, M.D., New Hyde Park, N. Y.

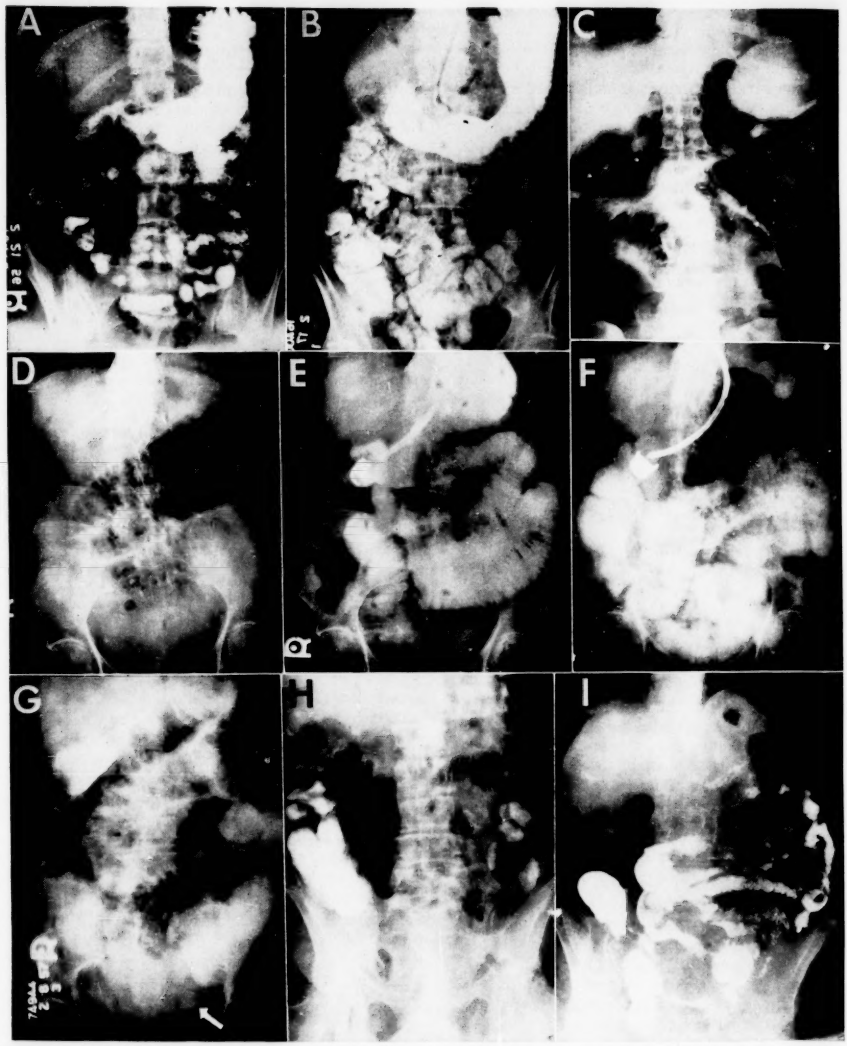
The interpretation of scout abdominal roentgenograms for intestinal obstruction depends chiefly on evaluation of intraluminal gas and fluid patterns. All too often it is assumed that this diagnosis is arrived at easily when gas and fluid levels or ladder patterns of distention are present in the small intestine. However, the difficulties and shortcomings inherent in this examination often are underestimated.

Opinion as to the use of barium sulfate suspensions for examinations of the small intestine when intestinal obstruction is suspected still is divided. Generally such examinations are considered hazardous when a complete or strangulating obstruction exists. The danger is regarded as less when there is only partial obstruction of the small intestine, provided that the colon is clear. Difficulty also may arise in the differentiation of distended loops of small intestine from dilated colon, particularly the transverse colon. Sometimes neither the configuration nor position of the distended loops permits their anatomic identification.

From the Department of Radiology, the Long Island Jewish Hospital.

Recently, the oral administration of water-soluble substances commonly used for intravenous urography and angiocardiography has been suggested for gastrointestinal examinations.[1] These substances are nontoxic, cannot solidify, and are unabsorbable from the gastrointestinal tract. I have used diatrizoate (Hypaque) sodium in dilutions varying from 30 to 90% and Renografin (a mixture of the sodium and methylglucamine salts of diatrizoate) in strengths varying from 30 to 76%. On request, diatrizoate was made available by its manufacturers in powder form and in bulk solution, which may be diluted and flavored as desired. Renografin was later supplied in bulk unsterile 60% solution for oral use. The main advantage of these preparations is lower cost.

In normal adults, good opacification of the stomach, duodenum, and upper jejunum can be obtained with solutions of either contrast medium in dilutions of from 30 to 90% (see figure, parts *A* and *B*). Weaker solutions are adequate for people of slight stature or for children. Good portrayal of the mucosal folds of the duodenum and proximal jejunum is obtained, but the mucosal pattern of the distal two-thirds of the jejunum and of the ileum often is indistinct. This is



A, abdominal roentgenogram, with patient supine, 15 minutes after oral ingestion of 60 cc. of 90% diatrizoate (Hypaque) sodium. Stomach, duodenum, and jejunum are well outlined, and some of contrast material has reached the ileum. *B*, film made one hour after oral ingestion of 90 cc. of 75% diatrizoate in another normal adult patient. Stomach contains considerable amount of contrast medium, although small intestine and colon have been traversed. This illustrates rapid transit time usually seen. Note lack of sharpness of mucosal pattern of small intestine. *C*, abdominal roentgenogram, with patient supine, one hour after oral ingestion of 30 cc. of 76% Renografin in patient with ileus secondary to acute ulcerative colitis. Contrast medium has collected and remained in gastric fundus. *D*, roentgenogram, with patient supine, showing distention of small intestinal loops in midabdomen of 70-year-old woman with abdominal distention and vomiting for two days. This was interpreted as consistent with obstruction in ileum. *E*, same patient 15 minutes after administration of 60 cc. of 76% Renografin through Levin tube. Distended loops are jejunal. *F*, same patient after four hours. Contrast medium still is mainly in jejunum, but some has entered ileum and ascending colon. This was diagnosed as partial obstruction. At operation, distal jejunum was adherent to and kinked against sigmoid by firm adhesions. *G*, anteroposterior roentgenogram three hours after oral ingestion of 60 cc. of 70% diatrizoate. Note distended jejunum, indicating partial obstruction. Narrowed segment is seen low in pelvis to left of midline (arrow). *H*, same patient, 24-hour film. Small intestine is empty, and contrast medium is in colon. *I*, same patient, four days later. Three-hour film after barium meal. Note stenotic loop in pelvis. This patient, a 48-year-old woman, had partial obstruction due to peritoneal metastases from omental sarcoma.

attributed to the hygroscopic quality of the contrast medium. The normal transit time of these substances through the small intestine is from 30 to 90 minutes. It is not uncommon to find the contrast medium in the stomach, the entire small intestine, and the colon within the same hour.

If the clinical picture suggests the possibility of obstruction of the small intestine and plain roentgenograms show an equivocal pattern of intestinal distention, information about the size and location of the various intestinal loops may be obtained by the use of these water-soluble materials without danger or inconvenience to the patient other than the distaste of swallowing a rather acrid medicine. The main purpose of this procedure is to help determine the location and extent of an obstructive process.

Oral administration of from 30 to 90 cc. of an adequate concentration of either diatrizoate or Renografin has proved helpful. With bedridden patients, it is important to move the patient about to make sure that the contrast medium does not collect and remain in the fundus of the stomach. If this cannot be overcome, the contrast medium may have to be instilled through a duodenal tube. When adequate passage through the duodenum is observed, it is quickly possible to identify the position, caliber, and rate of passage of the contrast medium through the small intestine. Subsequent films made at appropriate intervals serve to delineate the intestinal loops, which become partly opacified as the contrast medium traverses them.

This procedure was employed in 10 cases in which the clinical picture and the scout roentgenograms suggested the presence of either obstruction of the small intestine or ileus after operation (see figure, part *C*). The surgical procedures had been laparotomies for ovarian carcinoma, pancreatic carcinoma, ulcerative colitis, regional enteritis, and carcinoma of the ascending colon. The contrast medium traversed the small intestine within 90 minutes in these patients, eliminating the possibility that there was any significant degree of obstruction. Conservative treatment for ileus was effective.

There were four postoperative patients in whom the presence of obstruction of the small intestine due to adhesive bands was considered probable (see figure, parts *D*, *E*, and *F*). In these the opaque medium was retained in loops of jejunum and proximal ileum for four hours or longer. Subsequent films at 12 hours showed some of the contrast material in the colon, while the distention of the small intestinal loops persisted. In these partial obstruction was diagnosed. In three, conservative treatment was elected even though equally competent observers differed in their opinion as to whether operation was indicated. Reoperation was considered necessary in one patient five days after operation, and several bands partially occluding the distal ileum were severed. In this patient the contrast material traversed the small intestine slowly. Retention of some in the ileum over a 24-hour period suggested a partial obstruction.

In two cases, partial small intestinal obstruction was attributed to peritoneal carcinomatosis from ovarian malignancies, and in one a similar process was due to spread from an omental sarcoma. Scout films of the abdomen showed distention of the small intestine with numerous fluid levels. There was considerable delay in the passage of the opaque medium through the small intestine, indicating partial obstruction. In the third patient (see figure, parts *G*, *H*, and *I*), a narrowed loop of small intestine was visible to the left of the midline in the pelvis. This was considered the obstructive site. After six hours the contrast medium appeared in the colon. Because of this it was considered safe to repeat the examination with barium. Again there was delay in the transit of the contrast material, but several areas of stricture could be clearly identified, better than with the water-soluble substances. This suggested that diatrizoate or Renografin be used for preliminary studies and that more definitive examinations with barium can be done when necessary.

Two cases of carcinoma of the cecum presented as partial obstructions at the ileocecal valve. In both there was sufficient opacification of the cecum to identify the lesion. The obstruction of the small intestine was considered partial because some of the contrast material entered the colon after six hours. One patient responded temporarily to intubation. The lesion was overlooked, and obstruction recurred about two weeks later. The diagnosis of cecal carcinoma was confirmed at operation. In the second case there was marked distention of the entire small intestine. The ileocecal junction was narrowed and tapered. At operation this was found to be due to infiltration of the ileocecal valve with tumor.

Water-soluble substances may also be used for examinations of the colon when there is question as to advisability of using barium. Such doubt may arise in patients with intussusception or where the possibility of perforation of the intestine or prolonged retention of contrast material is anticipated.

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Summary

Water-soluble contrast mediums used for intravenous urography or angiocardiography may be helpful in the examination of the small intestine when the use of barium sulfate suspensions is considered hazardous. These may be regarded as preliminary studies and may be followed by barium examinations if patency of the intestine is established.

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The diatrizoate sodium used in this study was supplied as Hypaque sodium by the Medical Research Department of Winthrop-Stearns, Inc., New York, and the Renografin by the Squibb Institute for Medical Research, New Brunswick, N. J.

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APPARENT INCREASE IN FREQUENCY OF INFECTIONS INVOLVING TORULOPSIS GLABRATA

PROCEDURE FOR ITS IDENTIFICATION

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Occasionally, rare yeasts of medical significance are sent to me for identification. Among these have been three strains of Torulopsis glabrata (Anderson) Lodder and De Vries in the years 1938 to 1956. Since March, 1956, six additional strains of this species have been received, all from human patients including two with yeast septicemia. The well-known increase in infection caused by Candida albicans following the extensive use of antibiotics [1] suggests a possible similar relationship between infection by T. glabrata and the use of antibiotics. The object of this report is to describe how this species can be recognized. When it can be identified with certainty by medical technicians, all failures and successes in treatment of patients infected by it can be referred to a definite name rather than being accredited to an unknown yeast or, worse yet, to the wrong species. At present the yeast is so little known that it is not mentioned in the more prominent books on medical mycology. T. glabrata has remained almost unknown because it is much less common than the Candida species found on or in the body, and its ability to cause disease in laboratory animals is marginal.

Black and Fisher [2] isolated T. glabrata from a patient who had bronchopneumonia. The yeast was inoculated intraperitoneally into rats. The rats were killed after 5 to 10 days, and the yeast was cultivated from some of the organs. In both rats the omentum was contracted into a hard mass and contained some hard nodules. López Fernández,[3] in an article containing many photographs, reported on the pathogenicity of several strains of T. glabrata. Rabbits, guinea pigs, rats, and white mice were used, the mice being more sensitive and giving a more complete histopathological picture. Intravenous and intraperitoneal inoculations gave the most constant results. The most characteristic feature was the formation of nodular lesions with an intense elaboration of reticuloendothelial cells. The yeast cells were localized within the macrophages, to give a histopathological aspect which López Fernández stated was identical to that found in histoplasmosis.

Lodder and De Vries [4] injected intracardially five strains of T. glabrata from human sources into five rats each. Three of the five inoculated from one of the strains died in about three months. Two other rats died also, each having received injection of a different strain of yeast. The yeasts were isolated from the lungs of the dead rats. Lodder and De Minjer [5] injected T. glabrata into a number of mice and rats intraperitoneally and subcutaneously. No pathological changes could be observed in these animals, and yeast cells were never found in any of their organs. Lodder and De Minjer concluded that this strain was not pathogenic. There are good reasons for believing that all of the preceding papers were based on studies of authentic strains.

The results of tests in animals are certainly not the final indication of a strain's pathogenicity in humans when the results are weak and variable, but the recurrence of characteristic pathology after injection with some strains is strongly suggestive. The repeated isolation of the yeast in cases of septicemia in humans is strongly indicative, and over 60 positive cultures have been made from the blood of one patient. Just as the common use of antibiotics has increased the incidence and seriousness of infection by the very commonly carried C. albicans, so an increased incidence of human infection by the more marginally pathogenic species, T. glabrata and C. tropicalis, might be anticipated. Stovall and Pessin [6] have demonstrated that 5 to 15 times as many cells of C. tropicalis as of C. albicans are required to cause death in rabbits; and Seligmann [7] showed that a strain of C. albicans which was nonpathogenic for mice became lethal when cells were accompanied by 2 mg. of aureomycin. It should be of interest for someone to test the pathogenicity of T. glabrata and C. tropicalis accompanied by antibiotics.

Differentiation of Yeast Species

The following notations regarding the identification of fermentative yeasts that are more or less commonly found on or in the human body are given from the viewpoint of one who has worked with pathogens to a considerable extent but who has been concerned with the taxonomy of all yeasts to a greater extent. Three of the species in the table are of special interest: C. albicans, which is definitely known to cause disease, and T. glabrata and C. tropicalis, which are thought to be marginal pathogens. Sufficient information will be given concerning these three to permit their separation from all other species that might be expected on or in the human body.

I routinely use 38 carbon sources for the identification of yeasts, of which five were selected for the table. As few of the yeasts studied are pathogens, an incubation temperature of 25 C is used for a period of 20 to 24 days. The assimilation reactions are less variable than fermentation reactions, and only 0.5% of carbohydrate is required as compared with 2% for all fermentation tests except with the sugar raffinose, which requires 4%. Cornmeal agar or other mediums used for enhancing the development of hyphae may be used for colonies or dalmau preparations. The latter

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permit the direct microscopic observation of cultures growing in plates or on agar-coated slides. I have described the morphologic and physiological procedures mentioned here elsewhere.[8]

C. krusei at four to six days' incubation on commonly used mediums produces colonies which usually show hyphal tips in the moderately crowded portion of the Petri plate when the plate is held to the light with the bottom of the plate toward the observer. Large cells are present microscopically. This species ferments glucose strongly but has no action on trehalose, C. krusei is a very common saprophyte.

T. glabrata produces colonies which are smooth and show no hyphal tips. It causes gaseous fermentation of glucose and trehalose. No other species of yeast is known which ferments these sugars and does not assimilate maltose, sucrose, and cellobiose. T. glabrata is very rarely isolated from sources other than the human body. It is most commonly found in the urinary, intestinal, and respiratory systems but it is not found in the central nervous system. It is much more closely related to the Candida species discussed immediately below than to Cryptococcus.

*Diagnostic Reaction of Yeasts Which Produce Gaseous Fermentation of One or More Sugars and Are More or Less Commonly Associated with Human Body**

	Carbon Assimilation					Fermentation					
	Glucose	Galactose	Maltose	Sucrose	Trehalose	Glucose	Galactose	Maltose	Sucrose	Lactose	Raffinose ½†
Torulopsis glabrata	+	—	—	—	+	+	—	—	—	—	—
Candida krusei	+	—	—	—	—	+	—	—	—	—	—
C. parapsilosis	+	+	+	+	+	+	V	—	—	—	—
C. guilliermondii	+	+	+	+	+	+	V	—	V	—	V
C. albicans v. stellatoidea	+	+	+	—	+	+	—	+	—	—	—
C. albicans	+	+	+	+	+	+	V	+	—	—	—
C. tropicalis	+	+	+	+	+	+	+	+	+	—	—
C. utilis	+	—	+	+	+	+	—	—	+	—	+
Saccharomyces cerevisiae	+	+	+	+	+	+	+	+	+	—	+
S. fragilis	+	+	—	+	V	+	+	—	+	+	+

* + Means growth where it refers to assimilation, gas where is refers to fermentation; V means variable;—means no growth where reference is to assimilation, no gas where reference is to fermentation.

† Raffinose ½ indicated that hydrolysis proceeds only to the melibiose stage.

C. parapsilosis, C. (Endomycopsis) guilliermondii, C. albicans, and C. tropicalis occur close together taxonomically in the same phylogenetic line of species. C. albicans and C. tropicalis strains generally produce hyphae quite noticeably, C. parapsilosis and C. guilliermondii to a lesser extent. C. albicans and C. tropicalis are immediately distinguished by their fermentation reactions. C. albicans and its variety stellatoidea is the only species associated with the animal body that produces a gaseous fermentation of maltose and not of sucrose; it also is the only yeast found there which produces chlamydospores. C. tropicalis is almost unique in producing a gaseous fermentation of sucrose and an alkaline reaction in raffinose. Rare strains of Saccharomyces also have this combination of reactions on sucrose and raffinose, but they are very different from C. tropicalis in carbon assimilation reactions and they have not been reported from the animal body.

C. parapsilosis and C. guilliermondii show no definite difference in the table presented here, but nearly all strains of C. guilliermondii ferment sucrose, whereas no strains of C. parapsilosis do. The two species differ in their ability to assimilate cellobiose and raffinose, C. parapsilosis assimilating neither and C. guilliermondii assimilating both. C. guilliermondii has a rather wide range of variation. It is possible that a further study of mating type reactions [9] and biochemistry will show that C. guilliermondii is presently composed of more than one species. C. guilliermondii and C. parapsilosis are most commonly found in association with trees and in soil; C. tropicalis is common in soil and occasionally occurs in the respiratory tract, and C. albicans is almost exclusively found in the animal body.

C. (Torulopsis) utilis is a rare yeast usually found associated with the animal body or in plants producing bakers' yeast. It is readily differentiated from the other fermentative species in the table by its carbon assimilation reactions and by its ability to assimilate nitrate. Saccharomyces cerevisiae has been isolated from the vagina of diabetics and from lungs and mouths of patients. S. fragilis and its imperfect form, C. pseudotropicalis, are occasionally isolated from the body and are the only lactose-fermenting species found there. Cryptococcus neoformans and related species are differentiated from all of the preceding by their ability to synthesize starch and inability to cause a gaseous fermentation of sugars.

Summary

There is some indication that Torulopsis glabrata, previously considered to be slightly pathogenic or nonpathogenic, is now becoming more common and may in some cases cause serious infections. This paper is written to alert physicians to its occurrence and to inform technicians regarding its identification.

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COUNCIL ON FOODS AND NUTRITION

SYMPOSIUM ON NUTRITION IN PREGNANCY

The following announcement has been authorized by the Council on Foods and Nutrition.

PHILIP L. WHITE, Sc.D., *Secretary.*

A symposium "Nutrition in Pregnancy" will be held in Columbia, Mo., Oct. 11, 1957. This symposium will be sponsored by the Council on Foods and Nutrition with the cooperation of Boone County Medical Society; School of Medicine, University of Missouri; and Adult Education and Extension Service, University of Missouri.

The program, which will begin at 8 a.m. Friday, Oct. 11, will be held in the auditorium of the University of Missouri Medical Center. The meeting will be open to all interested persons, and there will be no registration fee.

The following program has been arranged:

Morning Session

8:00 a.m. Registration.

9:00 a.m. Influence of Maternal Nutritional Level on the Fetus and Infant. Dr. Ray Hepner, Associate Professor of Pediatrics, University of Missouri Medical Center.

9:30 a.m. Metabolic and Biochemical Changes in Normal Pregnancy. Dr. Icie Macy Hoobler, Consultant, Merrill-Palmer School, Detroit; Former Director, Research Laboratory, Children's Fund of Michigan.

10:30 a.m. Importance of Nutritional State of Mother Prior to Conception. Dr. Genevieve Stearns, Research Professor of Orthopedics, State University of Iowa.

11:15 a.m. Nutrition Experiments as an Instrument of Teratologic Research. Dr. Joseph Warkany, Professor of Pediatrics, University of Cincinnati.

Discussion: Dr. Albert G. Hogan, Professor Emeritus of Animal Nutrition, University of Missouri.

Afternoon Session

2:00 p.m. The Effect of the Reproductive Cycle on Nutritional Status and Requirements. Dr. William J. McGanity, Associate Professor of Obstetrics and Gynecology, Vanderbilt University, Nashville, Tenn.

2:45 p.m. Dietary Habits During Pregnancy. Miss Dorothy Vorhies, Associate Professor of Dietetics; Mrs. Barbara Birmingham, Nutritionist, Outpatient Department, University of Missouri Medical Center.

3:30 p.m. Panel Discussion to Review Epidemiologic Studies.

Moderator: Dr. Icie Macy Hoobler.

Participants: Dr. Samuel B. Kirkwood, Clinical Professor of Obstetrics, Department of Maternal and Child Health, Harvard University School of Public Health; Commissioner, Department of Public Health, Commonwealth of Massachusetts. Dr. William J. Darby, Professor of Biochemistry, Vanderbilt University School of Medicine. Miss Marjorie Heseltine, Chief, Nutrition Section, Division of Health Services, Department of Health, Education, and Welfare. Drs. Hepner, McGanity, and Stearns.

MEDICINE AT WORK

WORLD MEDICINE COMES OF AGE

FEARLESS CONCERN FOR PATIENT IS HIGH POINT OF HARMONY IN VOICES OF 700,000 DOCTORS

Milton Golin

Cuban police seize physicians as hostages. A "flu" epidemic finds the Philippine Medical Association in desperate need of drugs. Maltese doctors are threatened when they resist a move to limit patients' free choice of physician. . . .

These recent crises carry a direct threat to the general public, not to the medical profession alone. Ten years ago, doctors of each nation usually had to slug out such problems themselves. More likely than not, there was no place outside their borders to turn for help—no voice to bespeak their troubles or to forewarn their colleagues in other lands. Massive danger to health and medical practice was only part of the handicap to physicians and their patients 10 years ago. Doctors needed to know what scientific developments in Berne, Switzerland, could benefit clinical knowledge in Kansas City, or what new medical education precept discussed in Vienna might raise the proficiency level of an intern or a budding specialist in Melbourne.

Today medicine has an international voice, the World Medical Association, a confederation of 53 national medical associations representing more than 700,000 physicians around the globe. It is sounding an alarm against those who would oppress the doctor and his patient. It is telling the story of far-flung advances in medical science. It is rallying help for brother physicians who are in need.

Help was needed urgently last Memorial Day as Asian (Far Eastern) influenza was striking hundreds of thousands of Filipinos. Physicians were running out of antipyretics. Off went a frantic cable from the Philippine Medical Association to the World Medical

Association headquarters in New York City: "Request immediate airlifting of antipyretics, analgesics and if available polyvalent flu vaccine." The cable could not have arrived at a more difficult time. A long holiday week end loomed ahead, and many pharmaceutical firms either were closed or were operating with only stand-by staffs. Air transportation companies had their own priority problems. There was the prospect, too, of governmental red tape in an international drug shipment.

But WMA's secretary-general, Dr. Louis H. Bauer, and his staff tackled the problem with know-how. First they notified the Civil Aeronautics Board, and the red tape began disappearing. Then they found that officials of the Borroughs Wellcome & Company, Inc., of Tuckahoe, N. Y., were able to prepare a 300-lb. shipment of an antipyretic analgesic for delivery to Newark airport before 5 p. m. that day. From there, a Flying Tiger cargo plane rushed the supply to San Francisco, where a Pan American Airways plane was waiting to carry it the rest of the way. On Sunday morning, before the end of the holiday week end, the drugs were delivered to eager medical hands in Manila. The accomplishment was speedy, spontaneous, and completely voluntary.

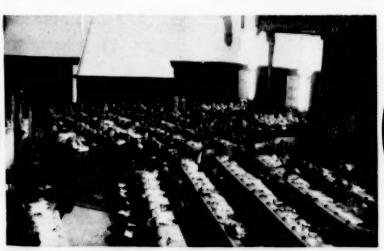
Within hours, other pharmaceutical firms were responding: A 600-lb. air shipment of analgesic from McNeil Laboratories; similar supplies arranged by E. R. Squibb & Sons; antibiotics and tranquilizers from Charles Pfizer & Company, Inc. Eli Lilly & Company launched a "crash" week-end project in their Indianapolis laboratories, in hopes of more quickly proving the effectiveness of their influenza vaccine. And Parke, Davis & Company authorized the Philippine Medical Association to obtain all necessary drugs from the company's Manila office. Said Dr. Bauer: "It is in the unity of purpose in such emergencies that the strength of the members of the health profession is tested—and proved equal to the task. It gives and does not count the cost; toils without resting; and asks no reward for its labor than a better and happier world for all people."

Help for Hungarians

Scores of Hungarian physicians certainly were asking no reward when they fled Communist butchery last fall. Many of them escaped so hurriedly that they left behind the vital papers which could show their accreditation. One of them reported: "I treated the children and youths injured in the rebellion. There was no time to fill in and file the numerous reports that the government required—nor did I feel justified in revealing the names, addresses, and conditions of the patients who came to me. . . . I was still in my clinic after midnight when a patient's mother came to warn me that the police were on their way to arrest me for treason. I fled. . . . I have no papers to prove who I am or what my education and experience has been—life, security, and freedom for my family were my only thought."

This doctor's plight illustrates a major project of the World Medical Association: A central repository for medical credentials (carrying the registrant's dated photograph, fingerprints, and notarized signature) so that physicians everywhere can prove their qualifications in case disaster strikes at their home country. "Success in this one program alone," says Dr. Bauer, "would justify the existence of WMA." For lack of such a repository, meanwhile, the WMA has been trying to establish new credentials for, and otherwise rehabilitate, Hungarian refugee physicians in the free medical world.

The WMA first spoke out against the Hungarian outrage last November in a telegram to the United Nations, strongly urging "that every necessary step be taken to prevent further butchery and deportation of Hungarian citizens and that the actions of those responsible for these atrocities be strongly condemned." Soon afterward, the U. N. did just that—censured perpetrators of the terrorism. Next came WMA's appeal to member associations and individual physicians that "all possible aid to Hungary through your organization . . . will be another proof of the importance the doctors of the world place on human dignity and freedom."



Left, international civil defense emblem (true color is red) which, if adopted universally, would identify and protect medical units in civil disaster, just as Red Cross marks units for safety during war. *Center*, World Medical Association's General Assembly in action at The Hague, Netherlands. This year's session will open Sept. 29 in Istanbul, Turkey. *Right*, official seal of WMA, which is observing its first decade of activity.

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Mature Voice of Medicine

This is the voice of world medicine, come of age, a voice with authoritative tone. WMA's cry against oppression in Hungary is the mature call of a young adult born out of the ferment of World War II. Doctors from many nations were thrown together in the common missions of that great conflict over a decade ago. Their wartime brotherhood in arms suggested the values of a permanent international alliance of organized medicine. These physicians also felt the need to restate medicine's universality, and to express their independence of political compulsions. There was a need, too, to assert a solidarity in repudiating the perverted medical practices which were forced against some physicians in Nazi concentration camps. (Based on a 1948 "Declaration of Geneva," WMA physicians pledge: "I will retain the utmost respect for human life from the time of conception; even under threat I will not use my knowledge contrary to the laws of humanity.")

In this background will the World Medical Association observe its 10th birthday on Sept. 18. When the WMA speaks today, it is heard as the official voice of the practicing profession, listened to by such diverse global agencies as the International Labour Office, International Social Security Association, and World Health Organization. And when WMA spoke out for help for Hungary's refugee doctors (sending 500 Swiss francs as a starter) it spawned offers of additional funds, medical supplies and aid, housing accommodations, and resettlement facilities from medical associations in the United States, Austria, Chile, Finland, Denmark, Cuba, and other nations.

Crisis in Cuba

The Cuban contribution, particularly, carries an ironic note. Even today, less than a year after the last WMA general assembly in Havana, Cuban physicians are being persecuted because they, like their Hungarian colleagues, gave medical treatment to those demonstrating against the government. Last June the Cuban Medical Association offices were raided during a regular business session. Physicians who care for sick and wounded "street rebels" still are being beaten, imprisoned and held as hostages. It is a criminal offense for the medical association to hold meetings.

The crisis in Cuba is scheduled for discussion at Istanbul, Turkey, starting Sept. 29 when WMA President J. A. Bustamante, himself a Cuban physician, opens the next general assembly under a theme of "Solidarity—the Key to Medical Advance." The WMA already has pointed out that, while doctors must fulfill their duties as citizens, they are pledged to serve humanity—without regard to religion, nationality, race, social standing, or party politics. Not long ago the WMA announced that while it cannot "within the framework of its constitution engage in political conflicts . . . the doctors of Cuba need the moral support of every freedom-loving medical association." Since then, letters of encouragement have been arriving daily in Havana, Santiago, and other Cuban communities, reminding the doctors that colleagues in other lands are supporting them in all humanitarian efforts.

Belgium and Malta

Repeatedly, humanitarianism has shown its power in the climate of world medical opinion. In Belgium, the government time and again has tried to create a state medical service which would force doctors to abide by all past and future ministerial regulations, and would require patients to obtain a permit before seeking medical care. So the Belgian medical profession organized its own medical insurance plan to assure free choice of physician. Not only are Belgian doctors and patients satisfied, but physicians from other countries have acclaimed the plan. This spring, WMA Delegate Pierre Glorieux reported: "My [Belgian] government, recognizing that it could not control the medical profession, sent a new bill to the parliament which . . . would remove all aspects of social security from the legislative power of parliament. The prime minister has officially stated that he will respect all the conventions of the medical profession."

Not long ago the territorial government of Malta embarked on a campaign of threat, insult, and harassment in an effort to limit the private practice of medicine in favor of a salaried service. When the nearly 200 Maltese physicians resisted, the prime minister hinted that he would import physicians from abroad to carry out his plan. The WMA promptly alerted the profession in neighboring countries, and the result was a governmental agreement to put aside its plans. Again, international solidarity among physicians had upheld a measure of freedom for them and their patients. (Says the WMA: "Confidence in one's doctor is essential for good therapeutics, and a patient does not ordinarily have confidence in a doctor whom he is compelled to consult.")

In scattered regions of the world other physicians are gaining strength and moral support from the World Medical Association:

—The Venezuelan government revamps its social security bill in order to include a free choice of doctor for the patient, after the Venezuelan Medical Association points out that "the best interests of the people and the profession can only be served when the legislation conforms to the Twelve Principles of social security established by the World Medical Association."

—The Japanese Medical Association arouses physicians in scores of nations when it reports in the trilingual (English, Spanish, and French) *World Medical Journal*, official publication of the WMA, that government medicine methods threaten to restrict visits of Japanese patients to their doctors "in complete disregard of public opinion."

—Bolstered by WMA principles, the Chile medical profession has achieved a new unity in its three-year battle against restrictive government pressures.

Other Programs

It would be a mistake, judging from these events alone, to regard WMA as a lobby bent only on fighting the evils of socialized medicine. Other efforts outshine its role as an alarm-ringer and fighter for unfettered medical practice. One is the drive for a central repository for medical credentials. Another is sponsorship of the first World Conference on Medical Education, in London in 1953 (the second is set for 1959 in Chicago). The WMA also has adopted a modernized Hippocratic Oath, as well as an International Code of Ethics. Already successful in some South American countries, WMA is continuing to help in the establishment of national medical associations elsewhere throughout the world. Currently, it is:

—Promoting a freer international flow of proved therapeutic agents.

—Formulating principles of cooperation between practicing physicians and public health officers.

—Promoting medical research.

—Observing and reporting on the activities of more than 23 other international organizations as they affect the practice of medicine.

Another WMA project is universal adoption of a special emblem that will identify and protect medical units in civil defense—just as the Red Cross symbol protects units during armed conflict. The civil defense design (see figure) has been agreed upon by a joint committee of International Medicine and Pharmacy, the WMA, and the International Red Cross; it already is ratified by several nations.

Do Not Confuse WMA with WHO

WMA makes a point of distinguishing itself from the World Health Organization. WHO is strictly intergovernmental public health agency created by the United Nations and supported this year by member nations to the tune of $13,500,000. The World Medical Association, on the other hand, is completely nongovernmental in its origin of national medical associations. Operating this year on a budget of only $165,000 (little more than 1% of WHO's whopping expenditures), WMA is the voice of the practicing profession and the individual patient. During its first five years, WMA was pledged $250,000 by joint action of the American Medical Association Board of Trustees and representatives of the pharmaceutical industry. This placed the fledgling organization on sound footing. Since then, a United States Committee, and supporting groups of other nations—comprising individual physicians, laymen, and corporate members—have provided backbone support to WMA through dues ($10 annually per person in the U. S.) and voluntary activity.

One result of this individual participation is a stark awareness that what happens to the freedoms of 200 doctors and their patients on the Island of Malta, or in another part of the world, can affect the futures of doctors and patients everywhere. The U. S. Committee, approaching this year's membership goal of 10,000, thus is made up of physicians who have taken the lead in realizing that there is just as much need for boosting WMA as for taking part in county, state, and national medical society activities. They know that health is a language that can be spoken everywhere. Last spring, for example, some 3,000 physicians from 48 nations including the Soviet Union kicked over all barriers of communication when they took part in an annual International Congress of Otolaryngology in Washington, D. C. The atmosphere was amicable because they had a common interest.

Similar rapport in the health field is taking place this week in Rome, where an estimated attendance of 1,000 American dentists at the Federation Dentaire Internationale is furthering President Eisenhower's People-to-People Program. That program is being pursued not only by the U. S. Committee of the WMA but also by:

—Thousands of U. S. armed forces medical personnel who care for local populations overseas.

—American doctors who take part in demonstrations of new techniques during visits to hospitals and clinics abroad, as a means of stressing the desire of the United States to share its scientific progress.

—Pharmaceutical companies which emphasize international good will in their world-wide contacts. One—Smith, Kline & French—now has television production crews assigned to film activities of American physicians abroad in private, missionary, military, foundation, and government practice. Next February the firm will present the story as a documentary, portraying doctors as U. S. ambassadors of good will in Japan, Korea, Hong Kong, India, Indonesia, Iran, Turkey, Ethiopia, France, and Guatemala.

Instrument of Peace

As Dr. Albert C. Holt says in his hospital office in Bombay: "We are representing the whole medical profession in America to these people. . . . If we fail, American medicine has failed in their eyes."

Dr. Gunnar Gunderson, who is President-elect of the A. M. A., and also a director of WMA's United States Committee, puts it this way: "We can add new meaning to the M.D. degree—Medical Diplomacy. World peace cannot be attained until we build peace into the hearts and minds of men. Since physicians are the most intimately acquainted with the physical and mental needs of their patients, they are the most logical engineers for this great moral reconstruction project. If we more than half million physicians assume this task on an individual, personal basis we may yet succeed where soldiers, statesmen and politicians have previously failed."

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THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

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Subscription price . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

ANTIBIOTICS IN VIRUS DISEASES

The threat of widespread virus disease in the form of Asian influenza makes it highly desirable to clarify thinking on the treatment of virus diseases. The Council on Drugs has prepared a statment, which appears elsewhere in this issue of THE JOURNAL, page 58, explaining the limitations of antibiotics in influenza and pointing out that their use in the primary treatment of this disease would be contrary to good medical practice. The principles involved, however, also apply to other virus diseases.

Evidence that thinking on the treatment of virus diseases has been confused can easily be gathered from conversations in public places, where it is not unusual to hear a person say, "I have a virus cold, and my doctor is giving me penicillin." There is also evidence to indicate that the misuse of antibiotics is not limited to the United States. Hennessen in Düsseldorf [1] reports that "the use of broad-spectrum antibiotics often begins before a diagnosis has been established." He shows that the action of antibiotics in disease differs radically from that of antiserums. An antiserum acts on a particular pathogenic organism or it does not act at all. If one excepts sensitization phenomena, it can be said that an antiserum which does no good at least does no harm.

Antibiotics, however, act differently. If the antibiotic in a given case encounters a resistant organism, its side-effects become in fact its only effects. This, says Hennessen, is the situation with all true virus diseases. With the exceptions of the large-particle viruses like trachoma and psittacosis, the viruses are resistant to the known antibiotics. As a result, medication with antibiotics in virus diseases violates the principle of *nil nocere*, for it is likely to result in substantial damage. A virus disease is a systemic infection. Its manifestations in various individual organs follow an actual viremia during which a patient's defense mechanisms must be considered as being under serious strain even if his symptoms are not alarming. At this stage the administration of chemotherapeutic drugs and antibiotics inevitably disturbs the physiological flora of his body, possibly to a grave extent.

Most of the organisms that normally populate the orifices and cavities of the body are sensitive to antibiotics; while these organisms tend to vanish under treatment with antibiotics, the orifices and cavities tend to become populated by organisms that are resistant and frequently pathogenic. There is hardly a clinic or hospital today, says Hennessen, that is not inhabited by therapy-resistant, pathogenic organisms. A superinfection by such nosocomial organisms therefore is actually favored whenever an antibiotic is used where it is not called for.

Various other circumstances conspire to increase this danger. Jensen [2] has reported the successive appearance of strains resistant to penicillin, to streptomycin, and to chlortetracycline when these antibiotics were being used preoperatively as prophylaxis against infections in thoracic surgery. Mikkelsen [3] reported similarly on attempts to use powerful antibiotics prophylactically before gastrointestinal surgery, especially in cancer patients. Micrococcic infections increased to an alarming extent. Whitlows and furuncles afflicted the nonmedical personnel of the hospital, and a 12-bed ward had to be evacuated because its occupants all developed abscesses. Kapp [4] similarly, after studying the effects of antibiotic prophylaxis in 250 patients undergoing so-called clean surgical procedures, found that such prophylaxis actually predisposed the patient to postoperative infectious complications. Hennessen points out that side-effects of antibiotics which are merely annoying in healthy people can be disastrous in the critically ill.

A real danger exists in the use of antibiotics in virus diseases, whether patients take antibiotic-containing remedies sold over the counter or whether physicians prescribe them before the proper diagnosis is made. The Special Committee on Influenza appointed by the Board of Trustees has

1. Hennessen, W.: Antibiotika und Chemotherapeutika bei Viruskrankheiten, Deutsche med. Wchnschr. **82**: 1206 (July 19) 1957.
2. Jensen, K. A., cited in Dangers of Using Antibiotics, Foreign Letters (Denmark), J. A. M. A. **164**: 1373-1374 (July 20) 1957.
3. Mikkelsen, O., cited in Dangers of Using Antibiotics, Foreign Letters (Denmark), J. A. M. A. **164**: 1373-1374 (July 20) 1957.
4. Kapp, D. F.: Antibiotic Prophylaxis in Unpredictable Infections: Medical and Surgical Fallacy, Guthrie Clin. Bull. **26**: 165-168 (April) 1957.

stated that there is some degree of justification for using antibiotics when secondary bacterial infections follow the primary influenza infection, as they often do. The principles that should be followed in that case are outlined in the statement by the Council on Drugs. As regards the primary viral infection, however, experience indicates that the logical procedure is the development of a specific, preventive vaccine.

FITNESS OF AMERICAN YOUTH

In June, 1956, the President of the United States called a conference to deal with the fitness of American youth, a matter which had been called to his attention through publicity given to research based on certain alleged tests of physical fitness. This conference was held at the United States Naval Academy, Annapolis, Md., and was attended by approximately 150 invited participants, including physicians, athletes, coaches, educators, public health personnel, representatives of organizations interested in amateur and professional sports, representatives of mass publicity media and persons interested in recreation, the outdoors, and the general topic for which the conference was called. Dr. Elmer Hess and Dr. W. W. Bauer attended, invited as individuals. The proceedings of this conference have been published and single free copies are available from the American Medical Association, Bureau of Health Education (for sale by the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C., price 25 cents).

These proceedings reflect a broad, constructive, and sane attitude toward total fitness, embracing not only its physical but its mental, emotional, moral, and social aspects. They commend the work already being done and recommend that good work be encouraged and that no new agencies be established, particularly at the federal level. Where serious gaps exist, community cooperation is recommended with a maximum of encouragement to existing agencies for the expansion and enrichment of programs already in action.

The presiding officer of the conference, the Vice-President of the United States, stated in effect that the American people are not a nation of "softies" but that considerable improvement in fitness can and should be expected.

The medical profession welcomes this renewed interest in fitness stimulated by the President's conference and the subsequent actions of the President as recommended by the conference. By executive order on the same day that the conference met and reported, the President created at cabinet level a council on youth fitness, consisting of the Vice-President of the United States, chairman, and six cabinet officers (the Secretaries of Defense, Interior, Agriculture, Labor, and Health, Education and Welfare, and the Attorney General). He also implemented a second recommendation of the conference, namely that there be an advisory committee to the President's Council and that this committee be composed of outstanding citizens. Five doctors are included in its membership (Philip S. Barba, W. W. Bauer, Daniel Bergsma, Martha M. Eliot, Hans Kraus). The Committee is meeting at West Point, N. Y., September 9 and 10, 1957.

Almost immediately, a director was appointed for the President's Council on Youth Fitness; he is Shane MacCarthy, J.D., a political scientist and lecturer identified with the Central Intelligence Agency. His functions are to coordinate the work of the council and to encourage activities in youth fitness.

All this has a familiar sound to the medical profession. The early proceedings of the House of Delegates of the American Medical Association have shown an interest in the fitness of American youth since the Association's organization in 1847. This interest took concrete form with the organization in 1911 of a Joint Committee on Health Problems in Education in cooperation with the National Education Association. This committee remains active and influential to this date and has to its credit a large number of publications which have influenced child health, including three books which constitute a trilogy in school health (Health Education, School Health Services, Healthful School Living).

During World War II, the American Medical Association, at the invitation of the United States government, participated in a Joint Committee on Fitness. The activities of this committee were in high gear when the war came to an end and the government withdrew its membership on the committee, leaving an American Medical Association contingent of five members. The then President of the American Medical Association, Dr. R. L. Sensenich, requested the Bureau of Health Education to make suggestions for a continuation of the Association's interest in health and fitness of American youth. The bureau proposed a plan for concentrating on the health of the school-age child as a key population group through which the greatest impact on the fitness of American youth could be made with the smallest amount of expense and largely through existing organization channels. This service was established experimentally in 1947, and an educator and a physician were added to the staff of the bureau to initiate the work.

For 12 years, the consultants in school health, augmented in 1956 by a woman physical educator, have ranged the highways and the byways of the

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United States giving aid, counsel, and cooperation in the development of statewide and local school health projects. Extensive improvements in measures for the protection and promotion of the health of school-age children have resulted and there is a ground swell of interest which promises to project this progress consistently into the future. The Association never presented a plan of its own, but was ready at all times to act as an exchange of information and a cooperating and counseling agency.

This fall, there will be held the sixth Biennial Conference on Physicians and Schools, which has become a traditional Highland Park Conference whose veteran participants belong to the "School Bell Club," having attended all conferences to date.

The Association also has had many other activities looking to the better health and fitness of American youth, including a broad program of health education, campaigns against quackery and charlatanism, the extension of rural health facilities, and medical service plans. Health and fitness aims are nothing new to the medical profession.

Physicians see in the renewed interest stimulated by the President of the United States an opportunity and a challenge. Fitness, according to the medical concept, must be based on essential fundamentals of which the first is good physical and emotional health.

To achieve this end, we must have good nutrition, periodic evaluation of health needs, follow-through efforts to meet these needs, intelligent attention to healthful living at home and in the school; adequate recreation and activity, the development of personal sports, and emotional adjustment to circumstances as they arise. A broad concept of fitness must not exclude the handicapped, who within their limitations must be helped to attain such measures of fitness as are available for them. Indeed, many a handicapped person stands as a luminous example to his fellows, through his achievements in the face of obstacles and discouragement.

Interest by the President of the United States has naturally stimulated great publicity. Everyone, with the remotest interest in fitness, has presented his viewpoint. This is the essence of a democracy and no one should wish that any of these voices be silenced. By the same token, however, the medical profession now faces a challenge to let its own voice be heard. The position of medicine with regard to the fitness of American youth should be clear and unequivocal.

Medicine stands for a broad concept of fitness, as indicated above. Medicine does not discourage activity, sports, competition, or even a reasonable risk of injury. Medicine recognizes that a fractured ankle may leave less of a scar than a personality frustrated by reason of parental timidity over participation in contact sports. Medicine does recognize, however, that there are contact sports which have for their main purpose, rather than competition and victory, injury to the opponent. Medicine recognizes also that there are contact sports and degrees of competition which are too severe for the immature. In standing out against the abuse of highly desirable exercise and highly necessary competition, medicine in no way objects to activity, competition, and risk, in its proper place. All life is a risk and without courage life is not worth living.

Medicine does deplore the fallacious use of the examination statistics from draft registration as a measure of health. These statistics do not take into account the voluntary enlistments nor do they consider deferments or exemptions from military service for reasons other than health; especially industrial, educational, and religious deferments. The statistics are based on fluctuating values and on essential military standards. They are a measure of military availability only and should not be quoted as indexes of the health of the nation's youth.

Medicine agrees with the Vice-President of the United States that American youth is not soft and decadent; it may be out of training but it has the basic health essentials for the quick acquisition of the necessary military skills. Height and weight figures show that our young people are stronger and heavier than any previous generation; the chances of a baby living to attend school are 96 in 100; the chances of a school child finishing his elementary and secondary education are 99 out of 100 on the basis of life and health, exclusive of economic and other considerations. Average length of life and life expectancy at birth are both at a high level. The conquest of diseases and disabilities affecting youth has brought into focus as our principal problem the conditions in the geriatric ages.

The medical profession may be counted upon as always to give its wholehearted cooperation to any worthy project embraced in the President's broad program for the fitness of American youth. By the same token, the medical profession will speak out without fear against any unsound proposals or against any movements which are wasteful, duplicating, and competitive to sound existing programs. The President's program conceived on a national level will be implemented largely on the local level. Physicians will be kept informed of developments through the columns of THE JOURNAL and other channels of communication. State and local medical societies have an opportunity and an obligation to make known to their communities their interest and willingness to participate in community action toward the greater fitness of American youth.

ORGANIZATION SECTION

DOCTORS, BROADCASTERS TO SPONSOR CONFERENCE

Representatives of medical societies, radio and television stations, voluntary health organizations, medical schools, and other allied groups are invited to attend a national conference on "How to Use Local Television and Radio in the Health Field" Nov. 7-8 at Chicago's Sheraton-Blackstone Hotel. The two-day conference is being sponsored jointly by the American Medical Association and the National Association of Radio and Television Broadcasters.

In announcing the meeting, Dr. David B. Allman, president of the A. M. A., and Harold E. Fellows, president of the N. A. R. T. B., said: "Public interest programs involving medical subjects are appearing more and more frequently on radio and television. Both broadcasters and physicians want to be sure that such programs are interesting, informative and factually correct. We hope that this meeting will enable those concerned to do a better job."

The fall conference will consist of a morning of general sessions on such topics as "Mutual Obligations in Public Interest Programming" and "How Accuracy and Good Taste Can Be Assured" and two half-days of section meetings. The sections, set up according to size of community, will discuss specific problems and offer broadcasters and medical representatives an opportunity to exchange ideas.

Only a limited number can be accommodated at the conference, so advance registration is advisable. Register by writing the American Medical Association, Department of Public Relations, 535 North Dearborn, Chicago 10, Illinois. No fee for the conference will be charged, but luncheon tickets will be sold.

HONOR FOUR DOCTORS AS ARTISTS

Four physicians, ranking among America's leading amateur artists, have been honored by the selection of their works for the first major national exhibition of professional-quality paintings by business and professional men.

Included in 38 selections by directors of seven major art museums are paintings by Drs. Joseph A. Falzone Jr. and Gustav Highstein, both of Baltimore; Frank Hinman Jr. of San Francisco, and W. Carl Lindstrom of Tulsa, Okla. Their works were previewed in Milwaukee and then placed on exhibit last June 15 in the Merchandise Mart in Chicago before being circulated by the American Federation of Arts on a two-year tour of art museums, leading universities, and civic centers.

Dr. Falzone is a research physician who has been painting for 12 years without benefit of formal art training. He has had award-winning paintings exhibited by the Society of Independent Artists and by the City Art Museum in St. Louis, the Pennsylvania Academy of the Fine Arts, and the Baltimore Museum of Art. Dr. Highstein, a pediatrician, has won two awards in annual exhibitions of the American Physicians Art Association and has been honored also in exhibits for Friends of the Museum, the Sweat Memorial Museum, the Baltimore Museum of Art, and the Corcoran Gallery of Art. Dr. Hinman started painting during World War II while he was a surgeon aboard an aircraft carrier. One of his prize-winning pictures was reproduced in color in *Life* in 1948. He is associate clinical professor of urology at the California School of Medicine. Dr. Lindstrom is an obstetrician and gynecologist who began taking color photographs, and then turned to painting, while serving as a surgeon in Italy during the last World War. For the past year he has been host to classes of professional men who paint as a hobby.

The current art show, entitled "From the Executive's Easel," is sponsored by Manpower, Inc., a nationwide temporary help service. The exhibition is described as "proof that business and professional people are producing exceptional work while utilizing painting as an escape from the strain of business activities."

NEW A. M. A. COMMITTEE ON AVIATION

The Council on Industrial Health of the American Medical Association is forming a permanent Committee to look into aviation medical problems. A decision to create such a body from an *ad hoc* special committee was implemented late in July by the Board of Trustees. It is hoped that members of the original group, headed by Dr. Jan Tillisch of the Mayo Clinic, will serve on the permanent committee. Investigations of the *ad hoc* committee had brought out: 1. There is an acute shortage of qualified air crew medical examiners. Two-thirds of the 180,000 examinations performed each year are done by family doctors. 2. Pilots disqualified for serious medical conditions—including coronary disorders, epi-

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lepsy, diabetes, psychoneurosis, and psychosis—have continued to fly. (One medical witness alleged that less than 1% of pilot medical certification is turned down for physical standards which would disqualify 25% of the general population.) 3. Although the five-member Civil Aeronautics Board proposes rules concerned with medical examinations, its organization has no doctor or medical staff.

Formation of the new A. M. A. permanent Committee on Civil Aviation Medical Problems was expected to be accomplished well before the next meeting of the parent Council on Industrial Health, to be held on Oct. 17, according to Council Secretary, B. Dixon Holland.

RURAL HEALTH MEETING IN OCTOBER

How to develop more effective rural health programs will be the chief topic of concern at the A. M. A.'s second study conference to be held on Oct. 4 and 5 for members of state rural health committees. Sponsored by the A. M. A. Council on Rural Health, the conference will again be held at Purdue University.

The opening session will be devoted to a discussion of organizational techniques of statewide rural health committees. Another session will feature representatives of leading farm organizations outlining their health programs. Following this latter presentation will be a discussion of ways that the medical profession and agricultural groups can best work together in developing better health programs. Reservations for this conference should be sent directly to the Student Union, Purdue University, Lafayette, Ind.

SIXTH NATIONAL SCHOOL HEALTH CONFERENCE

The theme of the sixth National Conference on Physicians and Schools to be held Oct. 30–Nov. 2 at the Moraine Hotel, Highland Park, Ill., will be entitled "A Decade of Progress in Fitness." Sponsored by the A. M. A. Bureau of Health Education, the program will emphasize a continuing interest in the health and fitness of children and youth.

More than 60 consultants and resource persons have been selected from the fields of medicine, education, and public health to lead the discussion groups on the physician's role in youth fitness; community coordination; mental and emotional aspects of fitness; dramatizing basic fitness procedures; medical guidance in girls' recreation programs; special health problems in athletics; fitness of school personnel; optimum fitness for youth with special health problems; home and family relations; and food factors in fitness.

As in previous conferences, state medical societies, state health and education departments, and national agencies concerned with school health and health education have been invited to send representatives. State societies should select their delegates and notify the Bureau as soon as possible. In addition, medical associations should encourage state health and education departments to send representatives so that a nucleus of well-informed persons from several professions can lend interprofessional leadership to school health activities within each state.

HOTEL RESERVATIONS FOR THE ANNUAL MEETING

SAN FRANCISCO, JUNE 23-27, 1958

For the convenience and protection of members of the American Medical Association, exhibitors, and guests, there will appear in the advertising section of THE JOURNAL as early as January, 1958, a list of San Francisco hotels, convention rates, and a room reservation form. The Housing Bureau has been instructed to give this form preference in the allocation of rooms that are reserved under contract with the San Francisco hotels, the Convention Bureau, and the American Medical Association.

Physicians attending the several pre-A. M. A. conventions (which are held during the prior week) are also expected to use this form to secure accommodations for the period of these respective pre-A. M. A. meetings.

CONFERENCE ON NUTRITION IN PREGNANCY

The A. M. A. Council on Foods and Nutrition has selected "Nutrition in Pregnancy" as the title of its 1957 symposium to be held Oct. 11 at the University of Missouri Medical Center, Columbia, Mo. Joint sponsors with the A. M. A. are the University of Missouri Medical School and Adult Education and Extension Service and the Boone County Medical Society. The symposium will provide an excellent opportunity for physicians, nutritionists, dietitians, nurses, and others to acquaint themselves with current findings in nutrition and the practical application of these findings to the management of obstetric patients.

Topics to be discussed include the influence of maternal nutritional level on the fetus and infant; metabolic and biochemical changes in normal pregnancy; importance of nutritional state of mother prior to conception; nutrition experiments as an instrument of teratologic research; the effect of the reproductive cycle on nutritional status and requirements; and dietary habits during pregnancy. Epidemiologic studies will be reviewed in a panel discussion.

SPECIAL COMMITTEE ON INFLUENZA

Report of the Council

The following report, prepared by the Council on Drugs at the request of the Special Committee on Influenza, is presented as a matter of scientific information for the medical profession.

HAROLD C. LUETH, *Chairman.*

ANTIBIOTICS AND INFLUENZA

The explosive outbreak of influenza during the past spring in the Orient, together with its erratic spread to Europe and the Western hemisphere, has recalled to the minds of many physicians the pandemic of influenza of 1918-1919. In the spring of 1918, a mild but widespread and explosive epidemic of influenza broke out in Europe. In many military units on the Western Front, the incidence of influenza reached a rate of 50% within a period of 10 days to 2 weeks. Certain civilian communities in Europe had comparable incidences of this mild type of influenza. The disease, in the spring of 1918, had a very low mortality rate and practically disappeared from the fighting forces and civilian communities by July 1, 1918. However, in September and in succeeding months influenza returned, and all communities in the world except those that were completely isolated (Tristan da Cunha, for example) were stricken by the infection. In its waves in 1918 and 1919, the disease was characterized by (1) a high morbidity rate, (2) an ability to injure the lungs, thus facilitating the invasion of micro-organisms which produced pneumonia, and (3) a high case fatality rate among those patients who developed pneumonia. It has been estimated that 20 to 30 million people died during this pandemic.

The influenza viral infection in the fall and winter of 1918-1919, while prostrating in effect, did not kill in itself except rarely. Pneumonia and its complications produced by beta-hemolytic streptococci, micrococci (staphylococci), pneumococci, influenza bacilli, and rarely by certain other organisms were responsible for the deaths.

There has been a close and disturbing parallel between the outbreaks of influenza which have been observed in Asia during the past spring and which spread to the Western world and the vernal appearance of what was called Spanish influenza in 1918. The question which is agitating the minds of many physicians at the moment is whether they will witness this fall a recrudescence of influenza throughout the world comparable in incidence and severity (as far as secondary infection is concerned) with that which occurred in the winter of 1918-1919.

Should this occur, what policies should guide the physician relative to the prophylaxis and treatment of secondary bacterial infection in patients suffering from influenza? After a careful consideration of this whole problem, the Council on Drugs makes the following suggestions:

1. Since sulfonamides and antibiotics have no therapeutic effect on the viruses of influenza, their use in the primary treatment of influenza would be contrary to good medical practice.

2. Antibacterial compounds such as sulfonamides or antibiotics should not be generally used in the prophylaxis of bacterial infection in patients ill with influenza. The prime reason for this recommendation is to prevent the development of disease-producing strains of micro-organisms which would be resistant to sulfonamide or antibiotic therapy. The secondary reason is to obviate the development of reactions of sensitivity or of direct toxicity to antibiotics or sulfonamides. The possible exceptions to this injunction are (*a*) pregnant women, debilitated infants, and older individuals, (*b*) patients being treated for other bacterial infections with sulfonamides or antibiotics who develop influenza, and (*c*) patients suffering from chronic, nonallergic respiratory tract disease.

3. All patients ill with influenza in whom it has been demonstrated that secondary bacterial infections have developed should be treated with a sulfonamide or antibiotic of choice. In general, the following recommendations can be made as to the choice of sulfonamides and antibiotics: (*a*) pneumococcic pneumonia: penicillin, broad-spectrum antibiotic, sulfonamide; (*b*) beta-hemolytic streptococcic pneumonia: penicillin, broad-spectrum antibiotic, sulfonamide; (*c*) influenzal bacillary pneumonia: broad-spectrum antibiotic; (*d*) micrococcic pneumonia: this will be a real problem because of the resistance of strains of these organisms to sulfonamides and antibiotics. Careful testing of the sensitivity to the various antibiotics of micrococci isolated from patients ill with pneumonia should be done and the choice of the antibiotic made upon data garnered from these tests. If the condition of the patient is so grave as to necessitate immediate therapy, massive intravenous doses of penicillin plus 1 Gm. of streptomycin per day may be administered while the results of antibiotic sensitivity tests are being awaited.

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Finally, a word of caution should be raised relative to the hospitalization of patients ill with influenza. It is the carefully considered opinion of the Council on Drugs that patients ill with uncomplicated influenza should be treated at home. It is a well-demonstrated fact that in many hospitals a high percentage of personnel such as doctors, nurses, and attendants may be carriers of micrococci which are resistant to antibiotic or sulfonamide therapy. A patient ill with primary influenza who is introduced into such an environment would certainly be in jeopardy of contracting a micrococcic pneumonia which could not be cured by antibiotic or sulfonamide therapy.

CURRENT STATUS OF ASIAN INFLUENZA

The following report has been compiled from late data furnished to the American Medical Association's Special Committee on Influenza by the Communicable Disease Center of the Public Health Service, U. S. Department of Health, Education, and Welfare. Progress reports on Asian influenza will be transmitted to the profession regularly as long as there is a possibility of an epidemic.

HAROLD C. LUETH, *Chairman.*

There appears to be an increase of influenza-like illness in further civilian groups. A school-centered outbreak has occurred in Mississippi and a housing development has been affected in California. A Florida community also appears to have experienced an increased incidence of influenza-like illness in the past week.

Outbreaks and cases of influenza due to Asian strains were confirmed during the period June 1-Aug. 22 in the following locations: California (San Francisco, San Diego, Monterey, Davis, San Mateo, Los Angeles), Virginia (Norfolk), Rhode Island (Newport), Hawaii, Ohio (Cleveland), Iowa (Grinnell), Utah (Salt Lake City), Kansas, (Topeka), Maryland, Kentucky (Louisville, Morris Fork), Pennsylvania (Valley Forge, Lancaster, Old Forge), Texas (Corpus Christi, Bexar County), Washington (Seattle), Nebraska (Omaha), Florida (Jacksonville, Miami, St. Petersburg), Michigan (Calhoun County, Bay County, Coldwater), Louisiana (Grant Parish, Tangipahoa Parish, New Orleans), New Jersey (Burlington County), New York (Cayuga County, New York City), Oregon.

Reactions to Influenza Vaccine Containing Asian Strain Virus

Of 239 volunteers vaccinated with monovalent Asian strain influenza vaccine, 158 were examined and questioned, for the purposes of this report, concerning postvaccination reactions. Injections were given intramuscularly over the deltoid area, and subjects were approached two or three days later. Vaccination groups included one each at 50, 100, and 200 CCA (chick cell agglutination) units and an equal number of saline and aluminum phosphate adjuvant subjects at each dosage level.

The volunteers were examined or questioned for evidence of local erythema and pain or swelling and any other postvaccination symptoms. *Any* affirmative reply was considered a positive reaction regardless of whether mild or severe. Care was taken to differentiate immediate injection pain and venipuncture discomfort from postvaccination signs and symptoms.

Reaction to Monovalent Asian Strain Influenza Vaccine

Reaction	% of 48 People Questioned After Dose of 50 CCA Units	% of 53 People Questioned After Dose of 100 CCA Units	% of 57 People Questioned After Dose of 200 CCA Units
Fever	6	8	14
Generalized pain in extremity*	21	23	54
Local swelling*	2	11	18
Local pain at injection site*	17	19	42

* Includes mild through severe reactions.

With the one exception noted below no severe reactions occurred. Symptoms were primarily those noted in the table and, with rare exceptions, lasted no longer than 12 to 24 hours. An increase in reactions was seen as the dosage of vaccine increased. Among those who had febrile reactions, only three were concerned enough to actually record their temperatures. Other symptoms mentioned in a few instances included malaise, myalgia, and headache. These were unrelated to dosage of vaccine. Differences in reaction to saline and adjuvant vaccines were not significant.

A single subject experienced sufficient fever, malaise, and myalgia to lose one-half day of working time. Otherwise, the symptoms noted were so mild that normal clerical activities were not interfered with or the subjects made unduly uncomfortable.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

In order to furnish the medical profession with a brief historical résumé of the factors underlying the development of Residency Review and Conference Committees as well as the significance of their role in the evaluation of graduate medical education, the Council has authorized publication of the following statement. EDWARD L. TURNER, M.D., *Secretary.*

BACKGROUND AND DEVELOPMENT OF RESIDENCY REVIEW AND CONFERENCE COMMITTEES

During the first two decades of the current century the Council on Medical Education and Hospitals of the American Medical Association was primarily concerned with the improvement of undergraduate medical education. Although it was apparent that this area would be a constant field of interest and concern, the Council recognized during the second and subsequent decades the need for increased emphasis on and improvement of advanced education and training beyond medical school. There was growing conviction in medicine that the learning process must continue throughout life and, as Ray Lyman Wilbur stated, "The doctor who stops learning goes backward."

Those concerned with undergraduate education during the earlier decades of the century were so deeply involved in its improvement that the medical schools themselves for many years evidenced little or no interest in graduate and continuing education. However, the terms "resident" and "resident physician" have been utilized in the United States for well over a hundred years, although at first they were more or less interchangeable with the term "intern." In 1889 Johns Hopkins Hospital instituted the use of the term "resident" to identify the young physician who, having completed an "internship," continued his training in a hospital so as to perfect himself in a special field of medicine. Thus at that time the educational aspect of graduate experience differentiated the resident from that of the salaried house officer whose function was to aid the medical staff in the care of patients, with little or no emphasis on graduate education.

During the 10 years following the Flexner Report, which appeared in 1910, along with the significant advances that took place in undergraduate medical education, increased attention was focused on education beyond medical school. The first major step in this direction was taken by the Council on Medical Education in the initial listing of hospitals approved for internship in 1914 and the survey of graduate medical schools and graduate education which it conducted in 1913-1915. As Johnson has stated, this survey and a subsequent one in 1919 indicated that the existing facilities for advanced training at that time were entirely inadequate. The demand by physicians for advanced training of high quality was not being met, proprietary schools and postgraduate schools of doubtful character were too plentiful, and there was little index of medical school interest in these fields.

Development of Specialty Boards

In 1917, to aid in insuring against the dangers of shortcuts to specialization, the ophthalmologists created the first of the specialty boards. This represented the first effort on the part of a specialty group to determine and uphold the basic requirements in education and experience needed to qualify as an acceptable candidate for examination and certification.

Wilbur reported that in 1919 there existed two large groups of physicians seeking study beyond medical school: those desiring continuing study for short periods and others who desired longer and more exacting preparation to fit themselves for special practice. Both groups involved a total of 10,000 physicians at that time. Approximately 6,000 were seeking short-term study and about 4,000 were engaged in prolonged training directed toward specialization. The Council became especially concerned with the latter group seeking to prepare for specialization, as it was felt that both the public and the profession should be protected against shortcuts to specialization, particularly in surgery, where abbreviated preparation was already being condemned.

Consequently, in 1920 the Council organized 15 committees of nine members each to study and "to recommend what preparation was deemed essential to secure expertness in each of the specialties." It is of interest to note that at that time 11 clinical and 4 basic science areas were included in the committee assignments. The clinical fields included: (1) internal medicine, (2) pediatrics, (3) neuropsychiatry, (4) dermatology and syphilology, (5) surgery, (6) ophthalmology, (7) otolaryngology, (8) orthopedic surgery, (9) urology, (10) obstetrics and gynecology, and (11) public health and hygiene. The basic medical science committees included: (1) anatomy, (2) physiology, (3) pharmacology and therapeutics, and (4) pathology-bacteriology. The 11 clinical fields and one of the original basic science areas subsequently have been included in the 19 American Specialty Boards which exist today.

The organization of these committees by the Council in 1920, therefore, essentially created the pattern underlying the establishment of the specialty boards in medicine and represented the forerunners of the American Boards. Initially the committees submitted widely divergent recommendations in regard to the minimum time requirements for specialization in the different areas. This varied from six months to three years, in contrast to the usual present-day requirements of three or more years beyond the internship. By 1923, the House of Delegates of the American Medical Association, on recommendation of the Council, adopted standards of specialty training referable to eligibility, program supervision, qualifications of instructional staff, and such factors as hospital, dispensary, laboratory, library, and museum facilities. The original statement in regard to the nature of instruction is of interest, for it included: "a) Review courses in anatomy, pathology and the other basic preclinical sciences which apply to the respective specialties; b) clinics in which students can have the opportunity personally to examine patients in hospital wards and outpatient departments and in which various therapeutic and operative procedures can be demonstrated; c) courses of operative and laboratory technic, and d)—to be assigned when the student's previous training will warrant—assistantship in which, *under the supervision of a physician who is recognized as an expert in the particular specialty, he can gradually assume responsibility in the diagnosis and therapeutic or operative treatment of the sick.* Opportunity should be provided also for research work in the chosen specialty bearing on both the fundamental sciences and clinical fields."

One of the most important features of this original statement is still the core of all sound programs of graduate education and training today, namely, the gradual upgrading of responsibility under competent supervision to the point where the physician on completion of his residency should be able to assume full professional responsibility in the diagnosis and in the determination of proper therapeutic procedures.

By 1928 these basic standards, after elaboration and redefinition, were incorporated into the documents of the Council and approved by the House of Delegates under the title of Essentials of Approved Residencies and Fellowships. The year previously (1927) the Council presented its first listing of hospitals approved by it for residency training in the various specialties. In that year, 278 hospitals provided 1,776 residencies. The significance and rapidity of development of specialty training is supported by the rapid growth of residency training since that time as summarized in table 1.

In 1933 the House of Delegates of the American Medical Association adopted a resolution authorizing the Council on Medical Education and Hospitals "to express its approval of such special examining boards as conform to the standards of administration formulated by the Council" and providing for the employment of the "Machinery of the American Medical Association, including the publication of its Directory, in furthering the works of such examining boards as may be accredited by the Council." The Council, therefore, was delegated the responsibility of approving on behalf of the American Medical Association those boards whose organization and administration meet with its approval. This responsibility was not limited to initial approval of an examining board but also to its continued approval by the Council as implied in the listing of such boards in the Directory of Approved Internships and Residencies and other official American Medical Association publications.

During 1933-1934 the Advisory Board for Medical Specialties was organized. From the beginning it has included representatives from each of the approved boards, to "act in an advisory capacity to such organizations as may seek its advice concerning the coordination of the education and certification of medical specialists." The Council on Medical Education and Hospitals has maintained close liaison with the Advisory Board for Medical Specialties through joint meetings and frequent conferences. During the past few years the Council and the Advisory Board have co-sponsored one of the major sessions at the Annual Congress on Medical Education and Licensure.

TABLE 1.—*Data Showing Rapid Growth of Residency Training Programs*

Year	No. of Hospitals	No. of Residency Positions
1927	278	1,776
1930	338	2,028
1935	392	2,364
1940	587	5,120
1945	736	7,666
1950	1,079	18,669
1955	1,201	25,841
1956	1,211	27,835

The "Essentials for Approved Examining Boards in Specialties" originally adopted by the House of Delegates in 1934, and as subsequently revised in keeping with developments indicates that the purposes and functions of a specialty board are: "a) To assist in improving the quality of graduate education in that field, b) to establish minimal educational and training standards in the specialty, in conformity with the general provisions of the 'Essentials,' c) to determine whether candidates have received adequate preparation as defined by the Board, d) to provide comprehensive examinations to determine the ability and fitness of such candidates, and e) to certify to the competence of those physicians who have satisfied the requirements of the board, as a protection to the public and profession."

The "Essentials" then outlined the general organization of a specialty board and the desirability of incorporation of specialty segments or subspecialties within the framework of major boards rather than developing independent boards. The "Essentials" also outlined the general qualifications of candidates for admission to specialty board examination and the mechanisms of establishing an acceptable specialty board, rendering approval in the specialties and basis for withdrawal of approval of a specialty board.

By 1949 there were 19 Approved Examining Boards in Medical Specialties as indicated in table 2. The American Boards of Internal Medicine, Pediatrics, and Surgery, in addition, certify in certain subspecialties and the American Boards of Obstetrics and Gynecology, Otolaryngology, Pathology, Preventive Medicine, Psychiatry and Neurology, and Radiology offer special certification in various areas of their respective fields. Table 2 indicates the names of the present approved examining boards in the medical specialties (1956), the date of their activation, total certificates awarded to June 30, 1956, and the various areas of special certification which have developed.

TABLE 2.—*Approved Examining Boards in Medical Specialties—1956*

Name of Board	Yr. of Activation	Total Certificates Awarded to June 30, 1956
American Board of Anesthesiology	1937	1,503
American Board of Dermatology	1932	1,713
American Board of Internal Medicine	1936	10,470
American Board of Neurological Surgery	1940	666
American Board of Obstetrics and Gynecology	1930	4,945
American Board of Ophthalmology	1917	4,464
American Board of Orthopedic Surgery	1934	2,731
American Board of Otolaryngology	1924	5,202
American Board of Pathology	1936	2,951
American Board of Pediatrics	1933	5,723
American Board of Physical Medicine and Rehabilitation	1947	302
American Board of Plastic Surgery	1937	359
American Board of Preventive Medicine	1948	1,684
American Board of Proctology	1949	246
American Board of Psychiatry and Neurology	1934	5,601
American Board of Radiology	1934	5,396
American Board of Surgery	1937	6,981
Board of Thoracic Surgery (Affiliate of the American Board of Surgery)	1949	625
American Board of Urology	1935	2,196
Totals		63,727
Certification in Subspecialties		
American Board of Internal Medicine		
Allergy		155
Cardiovascular Disease		503
Gastroenterology		354
Pulmonary Diseases		249
Totals		1,271
American Board of Pediatrics		
Allergy		71
American Board of Surgery		
Proctology		81*
Totals		1,423
Special Certification		Total Certificates Awarded to June 30, 1956
American Board of Obstetrics and Gynecology		
Obstetrics		22
Gynecology		13
Totals		35
American Board of Otolaryngology		
Endoscopy		4
American Board of Pathology		
Pathological Anatomy		1,467
Clinical Pathology		389
Pathological Anatomy and Clinical Pathology		1,059
Pathological Anatomy and Clinical Microbiology		1
Clinical Microbiology and Clinical Chemistry		1
Clinical Bacteriology		2
Neuropathology		12
Clinical Microbiology		14
Hematology		2
Clinical Chemistry		4
Totals		2,951
American Board of Preventive Medicine		
Public Health		1,219
Aviation Medicine		301
Occupational Medicine		164
Totals		1,684
American Board of Psychiatry and Neurology		
Psychiatry		4,298
Neurology		366
Psychiatry and Neurology		937
Totals		5,601
American Board of Radiology		
Radiology		3,635
Roentgenology		950
Diagnostic Roentgenology		544
Therapeutic Radiology		157
Therapeutic Roentgenology		4
Radium Therapy		7
Radiological Physics		47
X-Ray and Radium Physics		16
Medical Nuclear Physics		6
Totals		5,366

* Independent Board established in 1949.

Since the American Boards, as well as the Council, were concerned with the development of high-grade educational services, it was recommended in 1939 that a cooperative plan be developed for the joint study and appraisal of residencies and fellowships in the various specialties. This plan provided (*a*) that, after conference with the respective specialty board, a suitable application blank be prepared in triplicate so that one copy would be available to the Council, one to the specialty board, and one for the hospital files, (*b*) that an inspection be carried out by the Council's staff to confirm and amplify the information submitted by application, (*c*) that an inspection report be prepared emphasizing objective data that could subsequently be utilized in the evaluation of the educational program, (*d*) that copies of the application and inspection report be forwarded to the secretary of the board for further evaluation, and (*e*) that subsequently the application be submitted to the Council with the recommendation of the Board.

Most of the specialty boards soon entered into cooperation with the Council. In a short time all existing boards except ophthalmology were taking an active part in the study and evaluation of residency training programs. The American Board of Ophthalmology cooperated in supplying information to the Council but did not consider itself an evaluating or approving agency.

It is important, in connection with background information leading to the establishment of residency review and conference committees on graduate education, that the respective roles of the College of Surgeons and the College of Physicians, as well as the role of the Council on Medical Education and Hospitals, in improving and evaluating residency education and training be summarized.

Development of Conference Committee on Graduate Training in Surgery

Almost from its foundation in 1913 the American College of Surgeons evidenced interest and concern in the evaluation and approval of hospitals and in 1918 began its hospital standardization program. It employed a hospital inspection staff and pursued an application of more strict compliance with requirements pertaining to staff organization, hospital records, and staff meetings than was required by the Council for hospital registration at that time. The American College of Surgeons did not participate in the evaluations and approval of intern training programs. In 1928 the Board of Regents of the College of Surgeons indicated its interest and concern in graduate training in surgery from the standpoint of its relation to Requirements for Fellowship in the College as well as in relation to the provision of facilities to enable surgeons to achieve competency in surgery and the surgical specialties.

In 1937 the College of Surgeons instituted a survey of selected hospitals, and in January, 1939, it published a list of hospitals in the United States and Canada approved for graduate training in surgery. At the same time, a minimum standard was prepared which became known as "Fundamental Requirements for Graduate Training in Surgery." These "Fundamental Requirements" were oriented toward acceptable programs providing three or more years of organized, institutional graduate training—except in ophthalmology and otolaryngology in which two years were accepted if separate training programs were maintained. They also outlined the staff organization, educational committee, supervisory responsibilities, provision for basic medical science instruction, clinical facilities for both inpatient and outpatient activities, library, staff meetings, and conferences, etc.

The main differences between the Council's "Essentials of Approved Residencies and Fellowships" and the College of Surgeons' "Fundamental Requirements for Graduate Training in Surgery" at that time resided in the facts that (1) the American College of Surgeons approved only hospitals offering the full three-year program of residency training (except for ophthalmology and otolaryngology) and (2) in program evaluation the College placed greater emphasis on provisions for formal training in the basic medical sciences. During the period from 1937, the Council and the College conducted their respective programs and it was not until February, 1948, that a Joint Committee representing the American College of Surgeons and the American Medical Association met to discuss problems of mutual interest in this field of hospital surveys and the evaluation of graduate medical education and training. Representatives of some of the American Boards, the Advisory Board of Medical Specialties, and the Council on Medical Education and Hospitals of the American Medical Association were also present.

It was the sense of this general meeting that desirable economies of effort, time, and money could be accomplished if the American College of Surgeons and the Council on Medical Education and Hospitals of the American Medical Association would organize a single acceptable survey service which both organizations could support and be guided by and that, in addition, the joint procedure should be concerned chiefly with educational and organization programs of hospitals for residency training which should be supplemented by professional evaluation by the boards concerned. A subcommittee of the Joint Committee on Hospital Problems was appointed with representatives from the American College of Surgeons, the American Medical Association, the Specialty Boards (Orthopedic Surgery and Surgery), and the Advisory Board for Medical Specialties, which met in April, 1948. This subcommittee, in effect, became the forerunner of the Conference Committee on Graduate Training in Surgery.

Minutes of the Joint Committee on Hospital Problems held in July, 1949, include the following resolutions:

Resolved, That mutually acceptable standards of residency training in surgery and the surgical specialties be drafted by a committee appointed by the Chairman of the Subcommittee on Hospital Problems and representing the Council on Medical Education and Hospitals and the American College of Surgeons; *the standards so formulated to be referred to the appropriate bodies of the parent organizations for ratification.*

Be it further resolved, That a single uniform list of institutions approved for residency or graduate training in surgery and the surgical specialties be published by the Council on Medical Education and Hospitals and the American College of Surgeons. The Committee authorized in the previous resolution is also charged with formulating recommendations as to the specific procedures to be followed in preparing and publishing such a list.

Be it further Resolved, That the Chairman of the Subcommittee on Hospital Problems be authorized to appoint a committee to study ways and means of effecting a single survey service and that this committee report back to the Subcommittee on Hospital Problems at the earliest possible date.

After a series of committee meetings, conferences, and discussions, a meeting was held in May, 1950, attended by representatives of the American Medical Association, the American College of Surgeons, and the American Board of Surgery. The purpose of this meeting was to initiate the actions that had been given approval by the American Board of Surgery, the American College of Surgeons, and provisional approval of the Board of Trustees of the American Medical Association, as it was believed essential to get the coordinated residency approval program under way.

The minutes of this meeting clearly state that it *is the purpose of this conference to encourage the adoption by the sponsoring agencies of uniform standards for residency training in surgery, to sponsor a single inspection service for hospitals offering such training, and to approve and publish a list of acceptable residency programs.*

During the same meeting it was determined that the committee representing the American Board of Surgery, the American College of Surgeons, and the Council on Medical Education and Hospitals of the American Medical Association be called the Conference Committee on Graduate Training in Surgery.

The development of tripartite committees for the surgical specialties has been supported by both the Council and the College.

After further study and negotiation between the Council on Medical Education and Hospitals, the American College of Surgeons, and the American Board of Surgery, a "Joint Commission on Accreditation of Residencies in (General Surgery, Otolaryngology, etc.)" was recommended in 1953. Because of possible confusion from the use of the appellation "Joint Commission" the name reverted to the "Conference Committee on Graduate Training in Surgery." The Conference Committee on Graduate Training in Surgery is a tripartite committee with equal representation from the Council on Medical Education and Hospitals, the American College of Surgeons, and the American Board of Surgery. As currently agreed, the chairman and vice-chairman are representatives of the American College of Surgeons and the American Board of Surgery, with the provision that both of them

should not be from the same body and that the chairmanship should alternate between the organizations at intervals of two years. The secretary of the committee is a representative of the American Medical Association (currently a member of the staff of the Council on Medical Education and Hospitals as ex officio member).

Development of Residency Review Committee in Internal Medicine

In internal medicine the original movement to initiate a cooperative effort in graduate education and training stemmed from a meeting of the Board of Trustees of the American Medical Association and the Board of Regents of the American College of Physicians in April, 1939. Subsequently, plans for the formation of a Conference Committee on Graduate Training in Internal Medicine (now the Residency Review Committee in Internal Medicine) were developed in May, 1939, at a meeting attended by representatives of the Council on Medical Education and Hospitals, the American Board of Internal Medicine, and the American College of Physicians. The first organizational meeting was held in February, 1940. This Conference Committee appraised residencies through joint evaluation of hospital educational programs in internal medicine, meeting two or three times annually and functioning effectively and to mutual advantage until World War II interrupted its activities. During World War II the Council continued the approval of residencies in Internal Medicine in cooperation with the American Board of Internal Medicine.

A movement to reactivate the Conference Committee on Graduate Training in Internal Medicine originated with the American College of Physicians in 1947. At its meeting in June, 1947, and on two subsequent occasions, the Council on Medical Education and Hospitals voted to reactivate the Committee. In June, 1948, at the suggestion of the Board of Regents of the American College of Physicians and on invitation of the Council, a joint meeting was held in Chicago, at which time all three organizations (the Council, the College, and the American Board) agreed to reactivate the Conference Committee. The organizational meeting for Reactivation was held in February, 1949.

It is important to note that the two primary functions of this committee were indicated to be (1) the evaluation of residency programs in internal medicine, including new applications and reevaluation of approved programs, and (2) the establishment of standards for residency training in internal medicine. With regard to the latter, *the Committee's function was indicated to be recommendation to the sponsoring organizations.* Both Council and College agreed to these basic functions and the American Board of Internal Medicine in October, 1949, indicated its concurrence in granting authority to the Conference Committee to act also for it in the matter of residency approval and in the assignment of time credit for each residency.

In 1953 the Conference Committee on Graduate Training in Medicine officially changed its name to Residency Review Committee in Internal Medicine, in keeping with the belief that this name more adequately described its activities. This committee functions as a tripartite organization.

Residency Review Committees in Other Specialties

Obviously as an outcome of the development of the Conference Committee on Graduate Training in Surgery and the Residency Review Committee in Internal Medicine, there was increasing interest in the establishment of Residency Review Committees in each of the specialties with which the Council was collaborating. In the fall of 1952, therefore, a proposal was made to the Council that such committees or boards be developed in cooperation with each of the specialty boards, so that they could act for both groups in the approval of hospitals for residency training. It was proposed that each organization (the Council and the specific specialty board) would appoint representatives to the Residency Review Committee who would not necessarily be members of either organization but who would be specialists in the field concerned who were interested and experienced in residency training. The proposal suggested that administrative procedures for such committees be established in the office of the Council, which would have the secretarial representative, and that the chairman be selected from the Board representation in each instance. The proposal was endorsed by the Council and authority given to communicate with the Advisory Board for Medical Specialties and also with the respective boards (other than Surgery and Internal Medicine) as to their interest in such a development.

By May, 1953, five specialty boards had expressed their interest in establishing Residency Review Committees (orthopedic surgery, otolaryngology, pediatrics, proctology, and radiology), and subsequently committees have been established in all areas except obstetrics and gynecology, pathology and thoracic surgery. Although most of the Residency Review Committees are bipartite groups with representatives from the Council on Medical Education and Hospitals and the Specialty Board concerned, Internal Medicine, Surgery, and the Surgical Specialties of Otolaryngology and Plastic Surgery function as tripartite committees. Thus the Surgical Specialty Committees referred to also include representatives of the American College of Surgeons. The Council, in cooperation with the American Academy of General Practice, has established a Residency Review Committee in General Practice in an effort to assist in the elevation of graduate education and training in this field outside of the specialty areas.

The Residency Review and Conference Committees thus essentially represent cooperative partnerships through which the Council on Medical Education and Hospitals and the various specialty boards, the American College of Surgeons, and the American College of Physicians are endeavoring to conduct an objective and constructive program of accreditation in graduate medical education.

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MEDICINE AND THE LAW

FOREWORD

This is the first in a series of six articles dealing with the necessity for and proper format of certain medicolegal forms. The subjects to be covered are (1) consent to operations and other medical procedures; (2) patient's right to privacy; (3) confidential communications and records; (4) artificial insemination; (5) the physician-patient relationship; and (6) autopsy.

This material has been prepared and will be published in book form by the Law Department of the American Medical Association under the title "Medicolegal Forms with Legal Analysis." The book will include extensive legal citations and a substantial number of additional forms which have not been included in this series of articles.—ED.

Many physicians and hospitals throughout the United States do not follow the practice of requiring the signing of appropriate medicolegal forms in situations where experience has shown that the signing of such forms might have prevented a law suit. In other instances, inadequate medicolegal forms are in daily use. For example, "blanket" consent forms which purport to give the physician unlimited authority and discretion without specifying the particular operation contemplated are used extensively. The use of such forms has given rise to professional liability claims charging the performance of an operation different than the one for which consent was obtained. The courts have construed blanket consent forms to permit only the procedures which were orally agreed upon. In the absence of a consent form that describes within reasonable latitude the nature of the operation or treatment to be performed, a jury can very easily choose to believe the "forgetful" patient whose recollection regarding the treatment he authorized has been dimmed by time or circumstances.

In 1936, an article entitled "Authorization of Physical Examinations, Treatment, Operations, and Autopsies" by Dr. William C. Woodward was published in THE JOURNAL (**106**:33-40 [Jan. 4]). The present article and the five to follow have a twofold objective: (1) to expand and bring up to date the subject matter covered by Dr. Woodward and (2) to provide miscellaneous medicolegal forms of authorization and consent which physicians and their attorneys may adapt to their own needs.

In preparing these forms for publication, no effort has been made to provide complete uniformity, even with respect to details or format. Generally, the variations which exist do not have any particular legal significance. For example, some of the forms call for the addresses of the signer and the witnesses. Dependent upon local preference and circumstance, it may be preferable to include such addresses in a consent form. On the other hand, where the physician or the hospital already has this information in its records, it would be unessential. It may not be necessary to include the address of an employee witness since this information is usually available elsewhere. When the patient is accompanied by a friend or relative, it is a good policy to have this person sign as a witness and furnish his address, which may be stated either in the form or elsewhere in the patient's record. In these instances it is also desirable that an employee of the physician or hospital sign as a second witness.

If the patient is a minor, and someone else signs the form on his behalf, the relationship, if not apparent, should be stated in the consent form.

In our opinion, revised and up-to-date medicolegal forms should be available to physicians and should be executed by the patient in the physician's office, whenever circumstances permit, even though the hospital may also require the patient to sign similar consent forms. Local legal counsel should be consulted to make such changes in the suggested forms as are necessary to satisfy the laws of the jurisdiction.

Although the text and forms have been prepared to help physicians and hospitals, they are, at best, a poor substitute for competent local legal advice.

CONSENT TO OPERATIONS AND OTHER PROCEDURES

Assault and Battery.—Authority is necessary before a physician may legally examine or treat a patient. A physician who operates upon a patient without having authority to do so commits an assault and battery for which he may be prosecuted criminally or held civilly liable in damages. If the patient upon whom the unauthorized operation was performed is unable to prove that any actual damage was caused by the operation, he will usually be able to recover only nominal damages. However, the fact that the medical profession has not yet discovered the purpose served by the organ removed will not necessarily limit the patient's recovery to nominal damages; pain and suffering is an element of damages in assault and battery and some pain may be presumed to occur in the course

of any operation or in the course of recovering therefrom. It is no defense that the unauthorized operation was performed with due skill and care inasmuch as negligence is not an element of this cause of action. Authority for the performance of an operation may arise out of a legal duty or out of the consent of the patient or some one authorized to act in his behalf. In an emergency, authority is implied on the basis that it would probably have been granted.

Authority Provided by Law.—Some states provide, by statute, for the eugenic sterilization of feebleminded persons and habitual criminals. If the law under which the operation has been authorized is a valid, constitutional law, and if the procedure leading up to the order for sterilization has been in conformity with that law, and if the operation is performed in accordance with the law and without negligence, the physician authorized to perform the operation incurs no personal liability in performing it even over the objection of the person upon whom he operates. Similarly, statutory authority protects physicians in charge of state mental institutions, prison physicians, and health officers charged with the enforcement of vaccination and quarantine laws. The conduct of all such officers is subject to review by the courts. If they act beyond the scope of their authority, or if they act in an unlawful manner, they are liable for the payment of damages and may be subject to criminal prosecution.

Authority Provided by Consent.—Usually authority to operate arises from the valid consent of the patient or some one legally authorized to act in his behalf. It should be noted that even a valid consent is no defense in an action for professional negligence. The consent given may be either express or implied and, if express, it may be either written or oral. The consent given must be an informed consent with an understanding of what is to be done and of the risks involved. The procedure involved and its attendant risks should be explained to the patient in understandable nontechnical terms. The consent given may be invalid (*a*) because the act consented to is unlawful, or contrary to public policy, or (*b*) because the consent was given by one who had no legal right to give it, or (*c*) because it was obtained by misrepresentation or fraud.

In order for a consent to an operation to be valid, it must be the rational act of a qualified mind. The consent of the patient to the operation is sufficient, if he (*a*) has attained his majority and (*b*) is, at the time of giving consent, competent to understand the nature and purpose of the operation proposed and the risks involved. The consent of the husband to an operation on his wife is not necessary; the consent of the wife is sufficient authority. Nevertheless, it is advisable to have the spouse join in the consent whenever practicable. It is particularly desirable to do so if the operation involves danger to life, may destroy or limit sex functions, or may result in the death of an unborn child. A person who has attained his majority and is of sound mind is presumptively qualified to give or withhold consent. The presumption may be rebutted, however, by evidence showing that when the consent was given the party was drunk, or under the influence of drugs, or delirious, or comatose or otherwise incapable of exercising rational judgment. Under such circumstances the law will infer consent if the patient's life was at stake and there was no one present to give consent in his behalf. The fact that a patient is being treated free or at the expense of some one else does not do away with the necessity for obtaining his consent.

In agreeing to perform the operation, the physician does not, in the absence of a special contract, guarantee particular results or to cure. The physician warrants only that he possesses the degree of knowledge and skill ordinarily possessed by a member of the profession in good standing in the community and that he will use that knowledge and skill in the performance of the operation. Although admittedly an unsound practice, a physician may expressly agree to accomplish a particular result or effect a cure. If the physician enters into such a contract and fails to bring about the result or to effect a cure, he is liable for breach of contract even though he used the highest possible professional skill.

Invalid Consent.—Consent to a criminal abortion is void because such an operation is unlawful. Consent to an experimental operation that will greatly endanger the life of the patient and which is not intended to relieve or cure his illness or injury, but solely to advance the science and art of medicine, is usually regarded as contrary to public policy and therefore void. In theory, at least, the harm that might be done to society by such experimentation outweighs its possible benefits. Treatment involving an element of experimentation may properly be administered only with the full knowledge and consent of the patient or those legally responsible for him, and then only if the treatment does not vary too radically from the accepted methods of medical practice.

With reference to human experimentation, the House of Delegates of the American Medical Association in 1946 adopted the following statement set forth by the Judicial Council: "In order to conform to the Ethics of the American Medical Association, three requirements must be satisfied in human experimentation (1) the voluntary consent of the person on whom the experiment is to be performed; (2) the danger of each experiment must be previously investigated by animal experimentation, and (3) the experiment must be performed under proper medical protection and management." This statement, of course, assumes the legal prerequisite of therapeutic justification for the treatment undertaken.

An operation for sexual sterilization when such sterilization is not necessary for the cure or prevention of disease or antisocial conduct is generally regarded as contrary to public policy. This view finds strong support in the widespread legislation forbidding the indiscriminate dissemination of information

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as to how conception may be prevented and the indiscriminate distribution of devices and preparations designed for that purpose. Consent to a sterilizing operation is therefore probably void unless the operation is intended to cure or prevent disease or antisocial conduct or prevent a pregnancy that would endanger life.

Consent Obtained by Fraud.—Purported authority for an operation obtained by misrepresentation or fraud on the part of a physician is not valid authority and affords no protection to the physician. To represent to a patient that an operation is necessary to save life or to preserve health when that is not the case, or that it will give greater relief than there is any reasonable prospect of obtaining, is to perpetrate a fraud on the patient which vitiates his consent. Tactful honesty and frankness on the part of the physician are generally essential.

Minors.—Operations on minors, at least on those who have not attained years of discretion, may be lawfully authorized by the parents or, if there is no parent, by a guardian. If the minor has parents, consent should be obtained from them even though the minor is in temporary charge of some other person. In the instance where the parents are legally separated or divorced, consent on behalf of the child should be obtained from the parent who has legal custody. It is particularly important that consent be obtained when the procedure to which the child is to be subjected is for the benefit of some other person, such as a blood or skin donor.

It is not clear whether valid consent to an operation can be given by a child who has not attained his majority, although he is of sound mind and has attained the age of discretion. The fact that such a child is legally qualified to make a contract for medical services as one of the necessities of life may be construed as authorizing him to consent to an operation, at least when the cost is to be paid by him from his own funds. There may be a conflict, however, between the authority of the parent and the authority of the child, especially if a child is under treatment at the expense of his parents. Such conflicts seldom occur, but when they do they must be settled according to the circumstances of the case and the law of the community. In such cases, it is best that the physician refrain from action until the question of authority is settled, unless immediate medical attention is necessary to preserve the health or life of the child.

A man, and in many states a woman also, attains his or her majority on the day before the 21st anniversary day of his or her birth. In some states the age of majority for women is 18. Presumably, a woman would be regarded, in such states, as having reached her majority on the day before the 18th anniversary day of her birth. In some states the marriage of a minor "emancipates" the minor from parental control and may raise a legal question as to the relative rights of the parents or the emancipated minor where one or the other opposes the operation. In such a case the physician should not act without having first obtained the advice of competent legal counsel.

Consent is sometimes withheld by the parents on the ground that such treatment would be contrary to their religious beliefs or because of ignorance. Where the life or health of the child is in jeopardy, it is suggested that the physician or those interested in the child's welfare report the case to the local prosecuting attorney and to any available child welfare agency, with a view to having them initiate immediate legal action. There are statutes in some states which authorize the juvenile court to order necessary medical and surgical care for a minor whose parent or guardian, when able to do so, refuses to provide it. Pursuant to such statutory authority the courts have issued orders authorizing needed surgical operations and psychiatric examinations, despite the lack of consent on the part of the child's parents. In other states, courts, acting under the general statutes with respect to neglected and dependent children, have deprived the parents of custody and have appointed guardians authorized to provide necessary attention. Some courts have, however, refused to deprive parents of custody when they have refused to provide attention or treatment deemed by some to be necessary.

In determining whether to interfere with the parents' right to the custody and control of their child, the courts weigh the danger of the child's condition against the danger of the operation. Blood transfusions have been ordered, over the objections of the parents, for infants afflicted with an Rh complication. The basis for such court action is that there is only negligible danger in the transfusion while, without it, the child will almost surely die or, if it should live, its mental abilities will be greatly impaired. The court refused to order the amputation of a minor's abnormally large arm which was endangering her general health because the operation involved a serious threat to her life.

Incompetents.—Where the patient is of unsound mind and incompetent to understand the nature, the purpose, and the risks incident to a proposed operation, authority must come, (*a*) if he is a minor, from one or both of his parents, unless a guardian has been appointed for him by the court, in which case it must come from his guardian; or (*b*) if he has attained his majority, from his spouse or legally appointed guardian. An adult not under guardianship who is partially incompetent but sufficiently capable mentally of understanding his need for an operation and the possible consequences may be considered capable of assenting, especially in view of the fact that he is, despite his mental condition, considered in law to be capable of entering into a contract for medical services as a necessity of life. It is, nevertheless, desirable under such circumstances that a relative, or if there is none, some person who has demonstrated a genuine interest in his care and welfare, approve or join in executing the consent.

When an immediate operation is imperative and the patient is unable to consent rationally to the proposed operation, and when delay incident to the obtaining of the consent of some one legally authorized to consent on behalf of the patient involves serious risk to the patient, an operation may be performed on the legal theory of implied consent. The law implies that the patient would, if competent, consent to whatever may be necessary in his own interests. When a surgeon operates under such circumstances he should be prepared to show (*a*) that an immediate operation was necessary; and (*b*) that a lawful express consent could not be obtained from the patient or from any person authorized to act for him, without endangering the health or life of the patient.

Limits of Authority.—Ordinarily, an operation must be performed within the limits of the authority that has been given. The physician may not perform an operation different from that for which consent has been given. The operation must be performed in the manner which has been agreed upon. A consent must be obtained for each individual operation performed. A consent to one operation will not authorize another or later operation, even though the second operation is for the same condition as the first one. Authority may be given, however, for the operating physician to use his own judgment within certain reasonable limitations. It is usually mutually desirable for the physician to request the patient to allow him a reasonable amount of discretion in the performance of an operation. Even in the case of a limited operation, the operating physician must do whatever may be reasonably necessary for the safety of the patient. The ordinary legal implication is that if the patient under anesthesia had known beforehand of the circumstances that make a modification or extension of the operation necessary, or if at the moment he could exercise rational judgment, he would give his consent. Since it is assumed that the patient would consent to that which is for his benefit, the law implies consent in such cases. However, a physician may not, in the course of an authorized operation, perform a different operation or unauthorized supplementary surgery unless a true emergency exists; there must be a condition which if not corrected would be an imminent threat to life or could result in grave and irreparable injury to the health of the patient. It is not enough that the physician thinks that certain procedures will be beneficial to the patient. Also the physician must remember at all times that the patient's consent in no way relieves the physician of his duty to exercise due care in all that he does. Consent to the operation does not authorize any deviation from prevailing standards of care and caution.

Implied and Oral Consent.—An adult patient of sound mind, who knows that he can agree or refuse to submit to an operation, and who knows or has been fully and fairly informed by his physician as to what is to be done, and who then cooperates with the physician, has impliedly consented even though he has not consented in words. Such implied consent is the consent customarily given in routine office practice. Implied consent to operations always involves the possibility of misunderstanding as to the purpose and scope of the undertaking and the difficulty of obtaining proof in the event of a controversy. It is under the legal concept of implied consent that a physician is permitted, in an emergency, to operate on or extend the scope of surgery performed on an unconscious or delirious person who is unable to make his own decision. This situation frequently arises in connection with serious accidents when the patient is unable to act for himself. Of course, if some one is present who has authority to act for the patient or if, without jeopardizing the welfare of the patient, such person can be communicated with before operating, his consent should be obtained.

Oral consent to an operation is ordinarily supplemented by implied consent. For instance, a patient, after orally consenting to an operation, cooperates with the physician in its performance. Like implied consent, oral consent is open to misunderstanding and may be difficult of proof.

Written Consent.—While written consent to an operation is not required by law, it is desirable in order to avoid the misunderstandings that lead to lawsuits and also to facilitate proof when necessary. The prudent physician will demand a written consent or authorization with respect to any operation which involves an element of recognized danger to the patient or which requires hospitalization. No particular form is necessary to give validity to a written consent. The essential requirements are that it state clearly the nature and extent of the operation authorized and that it be signed by a person legally qualified to give consent. The authorization should state who is to be responsible for the administering of the anesthetic and the postoperative care of the patient if these services are to be performed by a physician other than the operating surgeon. The inclusion of the place and date of execution and the signature of a witness are desirable, but only because they tend to facilitate proof. Generally, the more vague and indefinite the terms of the consent, the more specifically it will be construed by the court. Care should be taken to spell out precisely and in the least technical language possible the exact procedure which the physician intends to perform or the particular condition which he seeks to relieve.

Authorizations and consents should be preserved at least for a sufficient period after the operation to cover the entire time within which, under the statute of limitations, a suit may be instituted. The length of the period of limitations varies from state to state.

Although the performance of an unauthorized operation is technically an assault and battery, it appears that an action for such an operation is

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sometimes governed by the statute of limitations as to malpractice or personal injury rather than by that as to assault and battery.

The physician would be wise to retain the authorizations and consents even after the expiration of the limitation period because the holdings of the courts are not uniform on the question of whether the statute begins to run at the time of the doing of the alleged wrongful act or at the time of its discovery. For minors the limitation period does not commence, generally, until the minor has reached his majority.

If a physician requests a written consent to surgery from the patient at the time the arrangements for surgery are made, the patient will be inclined to inquire as to his condition, the nature of the procedure contemplated, and the attendant risks. Under these conditions there can be no reasonable allegation by the patient later that he was under sedation when he signed the consent form, or that a hospital attendant had stated that the signing of the consent form was a "mere formality." Legally, the physician may rely for his authority upon a consent obtained by the hospital for his benefit, but it is readily apparent that the physician may protect himself best by attending to the details of having the consent form completed, signed, and witnessed in his presence. The use of business methods in dealing with this phase of medicine may reduce the number of liability claims that arise from misunderstandings, from the use of poorly drawn or antiquated medicolegal forms or from failure to use written forms.

FORM 1.—*Consent to Operation*

PATIENT ..... AGE .....

A. M.

DATE.....TIME.....P. M. PLACE.....

1. I hereby authorize Dr. ..... and whomever he may designate as his assistants, to perform upon ....., the following operation: .....

(State name of patient or "myself")

(State nature of procedure(s) to be performed)

and if any unforeseen condition arises in the course of the operation calling in his judgment for procedures in addition to or different from those now contemplated, I further request and authorize him to do whatever he deems advisable.

2. The nature and purpose of the operation, possible alternative methods of treatment, the risks involved, and the possibility of complications have been fully explained to me. I acknowledge that no guarantee or assurance has been made as to the results that may be obtained.

3. I consent to the administration of anesthesia to be applied by or under the direction of Dr. ....., and to the use of such anesthetics as he may deem advisable, with the exception of .....

(State "none", "spinal anesthesia", etc.)

4. I am aware that sterility may result from this operation although such result has not been guaranteed. I know that a sterile person is incapable of parenthood.

5. I consent to the disposal by authorities of the ..... Hospital of any tissues or parts which may be removed.

6. I consent to the taking and publication of any photographs in the course of this operation for the purpose of advancing medical education.

7. For the purpose of advancing medical education, I also consent to the admittance of observers to the operating room.

I CERTIFY THAT I HAVE READ AND FULLY UNDERSTAND THE ABOVE CONSENT TO OPERATION, THAT THE EXPLANATIONS THEREIN REFERRED TO WERE MADE, AND THAT ALL BLANKS OR STATEMENTS REQUIRING INSERTION OR COMPLETION WERE FILLED IN AND INAPPLICABLE PARAGRAPHS, IF ANY, WERE STRICKEN BEFORE I SIGNED.

Signature of patient .....
Signature of patient's husband or wife .....

When patient is a minor or incompetent to give consent:

Signature of person authorized to consent for patient .....
Relationship to patient .....

Witness: .....

Note. This is a general form of consent which will apply to various surgical cases by striking out the portions which are inapplicable. Where the anesthesia is to be administered by a nurse anesthetist, the name of the attending surgeon should be inserted in paragraph 3.

FORM 2.—*Consent to Disposal of Amputated Part or Organ*

I hereby authorize ..... to preserve for scientific purposes, or for use in grafts upon living persons, or to otherwise dispose of the following named tissues, parts, or organ, ..., of ...., in a proper and suitable manner.

(Name of patient)

Signed .....
Date .....

Witness .....

FORM 3.—*Consent to Treatment*

I, having been fully informed by Dr. ..... of the risks and possible consequences involved in treatment by means of ..... for the relief of ....., nevertheless hereby authorize Dr. ..... to administer such treatment to me, and agree to hold him free and harmless for any claims, or suits for damages for any injury or complications whatever which may result from this treatment.

Signed .....
Date .....

Witness .....

Note. This is a general form of consent that is intended for use, primarily, in connection with the administration of hazardous drugs and treatment normally provided in the physician's office.

FORM 4.—*Consent to Diagnostic Procedure*

PATIENT..... AGE.....

A. M.

DATE.....TIME.....P. M. PLACE.....

I hereby request and authorize Dr..... and whomever he may designate to assist him to perform upon ..... the following diagnostic procedure: .....

(Name of patient or "myself")

I have been fully informed of the risks and possible consequences involved and that unforeseen results may occur.

Signed .....

The foregoing consent was read, discussed, and signed in my presence, and in my opinion the person so signing did so freely and with full knowledge and understanding.

Witness .....

FORM 5.—*Agreement for Blood Transfusion*

To: Dr. .....

(Attending physician)

and.....Hospital. Date.....19.....

1. I hereby request and authorize the administration of a blood transfusion to .....

(Insert "myself" or name of patient)

and such additional transfusions as may be deemed advisable in the judgment of Dr....., the attending physician, or those he may designate to assist him.

2. It is understood and agreed that the attending physician or his assistants will be responsible only for the performance of their own individual professional acts, and that the blood typing and the selection of compatible blood are the responsibilities of those who actually perform the necessary laboratory tests.

3. It has been fully explained that blood transfusions are not always successful in producing a desirable result and that there is a possibility of ill-effects such as the transmission of infectious hepatitis or other diseases or blood impairments.

4. Also, it has been explained that emergencies may arise when it may not be possible to make adequate cross-matching tests, and that immediate need may make it necessary to use existing stocks of blood which may not include the most compatible blood types.

5. It is understood and expressly agreed that the blood supplied in accordance with this agreement is incidental to the rendition of services and that no requirement, guarantee, or warranty of fitness or quality shall apply.

Signature of patient .....

When patient is a minor or incompetent to give consent:

Signature of person authorized to consent for patient .....

Address .....

Relationship to patient .....

Witness: Signature .....

Address .....

City and State .....

COUNCIL ON MEDICAL SERVICE

THE ROLE OF EXERCISE IN THE AGING

Paul D. White, M.D., Boston

This is the third of a series of papers on various aspects of aging. Each paper has been prepared for the Committee on Aging by an authority in the field. When completed, the series will be published in booklet form.

As I sit down to write about the role of exercise in the aging, I am conscious of the pleasant and relaxing effect of a brisk walk in the clear cold air of Santa Fe and the hills around. As a senior member of society, I can vouch for this particular positive effect of exercise; for many aging persons this may be its chief value. However, there are other physiological results of exercise which deserve as much emphasis in the aging as they do in the young, and possibly even more.

Though such effects of exercise are frequently referred to in the presentation of health programs, they are but little discussed in planning for the health and happiness of older persons. To be sure, no hard and fast rules about exercise can be laid down for everyone of a certain age, in the first place, because no two persons have exactly the same physical needs or psychological preferences and, secondly, because chronological age is not the same as physiological age. Also it is true that some individuals live to be old and free from disease despite the fact that the only exercise they get is in breathing, eating, talking, and in tending to their minimal physiological processes of other nature; what percentage of healthy older persons belong in this category has not been determined, but it appears to be considerably in the minority.

Naturally, in extreme old age, when physical strength and mental ability steadily decline, there comes a time when exercise beyond that of the simplest acts of living is no longer possible, but in the early and middle years of old age exercise can be very beneficial. It is important to recognize that there is a difference between positive health and the mere absence of disease.

At any age, physical exercise, more or less planned, though not as a burdensome or boring program, has certain beneficial effects which can be helpfully reviewed in our discussion of the problems of aging. The kind of exercise is not very important except that it should suit the strength, aptitude, and liking of the particular person. It may vary in strenuousness from that involved in simple deep breathing in short periods several times a day to that involved in heavy wood cutting or snow shoveling or fast tennis.

There should be no age set at which a person long accustomed to vigorous exercise should cease exercising, although it is usually wise to tone down the energy expenditure and the amount of time per day or week with each passing decade. If a man or woman is in good health and enjoys exercise in the open air (or perhaps even if not) the beneficial effects can continue to a very advanced age. I have known of Maine guides and lumbermen, gardeners, sailors, laborers, and sportsmen who have kept up a vigorous program both enjoyably and beneficially well into the 80's.

There are very few adequate statistics concerning the health and longevity of athletes. Some articles and books have been published on the subject; one of these, entitled "University Oars," was written many years ago (1873) by Dr. John E. Morgan, who was an oarsman himself. Dr. Morgan, of Oxford University, made a follow-up study of members of the crews who took part in the annual races between Cambridge and Oxford from 1829 to 1869. His conclusion was that the effect of the rowing was a favorable one, that this type of exercise (some of which was continued for years afterward) had no unfavorable effect on health

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Members of the Committee on Aging are Drs. H. B. Mulholland, Chairman, Charlottesville, Va.; Edward L. Bortz, Philadelphia; Henry A. Holle, Austin, Texas; Wingate M. Johnson, Winston-Salem, N. C.; Theodore C. Klumpp, New York; Frederick C. Swartz, Lansing, Mich.; and Cecil Wittson, Omaha. Committee Staff: Mr. George W. Cooley, Secretary, and Mr. Herbert B. Norton, Research Assistant.

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but rather the reverse, and that the longevity of the oarsmen was slightly greater than that of the average population.

A study not yet reported, which my associates and I made, was a follow-up of Harvard football players who earned their letters between the years 1900 and 1930. This study showed a longevity close to that expected in the population at large. It had been hoped to compare those who continued vigorous exercise throughout their lives with those who took no particular exercise after graduation from college and also those who had gained very much weight with those who had gained practically no weight at all. Evidence on these two points was definitely favorable for those who continued vigorous exercise and who did not gain weight, but the numbers in these extreme groups were hardly adequate for statistical conclusions. One of the difficulties in such a study is that the majority of American males live a standard existence, that is, they eat much the same diet, drink and smoke moderately, get some exercise but not of any considerable degree, and gain a moderate amount of weight through the years (10 to 25 lb. or more in the course of 30 years).

Benefits of Exercise

Exercise has positive effects on the health. In the first place, there is the benefit of establishing or maintaining the general muscular tone throughout the body, including that of the heart itself. Some muscles, of course, become stronger if they are more involved in the exercise, for example, the leg muscles in long walks, golfing, cycling, or tennis, or the arm muscles in wood cutting, gardening, fishing, or housework. One of the muscles that it is important to keep in good tone is the diaphragm; almost any vigorous exercise or even repeated programs of deep breathing will help here.

There are several values that are derived from good muscle tone. One is that which concerns the circulation of the blood itself. Sometimes one forgets that the heart, although the most important factor of course, is not the sole supporter of the circulation. The elasticity of the aorta and other great arteries is of importance in maintaining an even flow of blood. The vasomotor function of the smaller vessels is vital for the selective distribution of the blood to the organs as needed. The peripheral veins with their valves act as local pumps for the return of blood to the heart when they are compressed by the muscles that surround them. The better the tone of the muscles the better is this support to the heart afforded by the veins. For the same reason, peripheral venous stasis of high degree with the development of varicosities, the pooling of blood, and phlebothrombosis is counteracted, to a certain degree at least, by good muscle tone. Finally, good tone of the diaphragm with wide respiratory excursions (aided by the avoidance of obesity) not only greatly helps respiration but also improves the pumping action of the diaphragm in its suction of blood back to the chambers of the right side of the heart.

A second benefit from exercise is that already referred to, namely, its effect on the psyche. Most individuals, old as well as young, are much helped by the relaxation which comes from exercise of the right degree, usually midway in amount and intensity between the extremes of triviality and of exhaustion. For many of us, exercise is a delightful antidote for nervous tension and strains, anxiety, and mental concentration. A pleasant fatigue of the skeletal muscles has time and time again given me mental repose, peaceful sleep, and a sense of equanimity.

A third benefit has been on digestion, partly, in all probability, by reducing nervous tension, which is a common factor in cases of esophageal irritability (cardiospasm) and peptic ulcer, and partly by its favorable effect on the bowel function.

A fourth benefit of exercise at any age, and therefore applicable to the "aging," is its favorable effect in helping to control obesity, a condition widely regarded as inimical to the best of health and longevity. Although it is true that obesity is due to the combined effects of heredity and overnutrition, nevertheless, with the same caloric intake, the increased metabolic requirement resulting from exercise does help to control body weight. It is not the fat deposited under the skin here and there throughout the body or in the omentum that is of most importance but rather a few grams of fat in the wrong places, particularly in the walls of the coronary and other important arteries.

Finally, the deepening of respiration which comes with exercise favors the function of the lungs in gaseous exchange and in the state of the lung tissue itself. Although chronic bronchitis and emphysema are common in old age and limit the amount of exercise possible, they are not a bar in themselves to mild exercise within the reserve of the person affected.

Even in the presence of disease other than in the lungs, suitable exercise can be beneficial. I have seen many patients with heart diseases of various kinds and degree and, except for the most severe cases, slight to moderate exercise can and should be prescribed. Of course, angina pectoris too easily induced or myocardial weakness of considerable degree will demand pro tem absolute rest, but with recovery or in the presence of well-healed myocardial infarction, as in the President's case, a careful program of regular exercise may not only be an important health measure but it may conceivably be helpful, in the absence of important symptoms, in retarding the further progress or increase of coronary atherosclerosis. Further research as to this possibility is in order.

Thus, in conclusion, it may be said that exercise of almost any kind, suitable in degree and duration for the particular individual concerned, can and does play a useful role in the maintenance of both physical and mental health of the aging individual but that no hard and fast rules can be set, because each person requires individual appraisal.

MEDICAL NEWS

ARKANSAS

State Medical Election.—The Arkansas Medical Society has recently installed Dr. T. Duel Brown, Little Rock, president; Dr. Louis K. Hundley, Pine Bluff, president-elect; Dr. John W. Smith, Little Rock, treasurer; and Dr. John J. Monfort, Batesville, secretary.

CALIFORNIA

Personal.—Dr. Frederick M. Kriete, assistant chief of preventive medical services with the State Health Department, has been appointed deputy state health director. The position was created at the last session of the Legislature. Dr. Kriete has been with the department since 1947.

Grants for Heart Disease Research.—Allocations totaling $221,669 for heart disease research have been announced by the Los Angeles County Heart Association. The grants are for support of 34 projects at Southern California School of Medicine, University of California Medical Center, College of Medical Evangelists, the Veterans Administration Center, and Cedars of Lebanon, Children's, and Los Angeles County hospitals. The majority of the studies are concerned with the cause and prevention of heart disease. Grants to University of California investigators working at the Medical Center, the VA Center, and Cedars of Lebanon Hospital total $112,927, including a $50,000 grant for the Heart Association Laboratory, where Wilfried Mommaerts, Ph.D., is studying the basic chemistry of the heart muscle.

Psychiatric Society Founded.—Twenty psychiatrists from Santa Clara and Monterey counties met at the Santa Clara County Hospital recently to officially form the Santa Clara–Monterey Counties Psychiatric Society. The purpose of this group will be to promote psychiatry in these two counties by sponsoring scientific-educational programs, by representing psychiatry in the community, and by encouraging fellowship between psychiatrists and workers in related fields. The society plans to become an affiliate society to the American Psychiatric Association. At the founding meeting a constitution was accepted and the following officers were elected: Dr. Robert A. Hall, San Jose, president; Dr. Fred Tempey, Agnews State Hospital, vice-president; Dr. Alan M. Clarke, Los Gatos, secretary-treasurer; and Drs. Raymond L. Hack, Salinas, Norman Rogers, Agnews State Hospital, and Walter J. Freeman, Los Altos, councillors.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

COLORADO

Automobile Crash Injury Study.—A unique study of automobile accidents has been initiated in Colorado primarily concerned with determining the nature and specific causes of injury to occupants of passenger cars. This program, known as Automotive Crash Injury Research, has been endorsed by the House of Delegates of the Colorado State Medical Society and will constitute a coordinated effort on the part of the society and the Colorado State Patrol. The study will function for a year as part of a 15-state program coordinated by the Automotive Crash Injury Research project of the Department of Public Health and Preventive Medicine, Cornell University Medical College, New York City. The Colorado study will help to evaluate the effectiveness of specific design changes in 1956, 1957, and 1958 model automobiles, energy-absorbing steering wheels, seat belts, and interior padding. Medical and accident data-collecting methods operate in the following way: all 1956, 1957, and 1958 passenger cars involved in injury-producing accidents outside the limits of municipalities come within the scope of the study. Immediately following an accident, the Colorado State Patrol officer in charge submits to the physician or emergency room chief or coroner a special medical report form furnished by Cornell which includes a description of the extent and nature of all injuries. Completed forms are mailed to the Colorado State Medical Society. These studies are sponsored by the Armed Forces Epidemiological Board through its Commission on Accidental Trauma, with funds supplied by the Surgeon-General of the Army, by the Division of Research Grants of the United States Public Health Service and by grants to Cornell University Medical College of unrestricted funds by the Ford Motor Company and the Chrysler Corporation.

CONNECTICUT

Dr. Paul Receives Lyman Medal.—The David Russell Lyman gold medal for "outstanding productiveness and service to public welfare" was awarded to Dr. John R. Paul on May 25. The presentation was made at the 55th annual meeting of the Gaylord Farm Association in Wallingford. Dr. Paul is professor of preventive medicine in the Yale Medical School, New Haven. In 1938 he and the Yale Med-

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ical School received the first research grant issued by the National Foundation for Infantile Paralysis. In making the presentation, Dr. Gustaf E. Lindskog, professor of surgery at Yale, said "Dr. Paul's interest in poliomyelitis and other neurotropic diseases, his outstanding accomplishments in rheumatic heart disease, appears to us to appropriately symbolize the changes and broadening emphasis now occurring at Gaylord Farm."

ILLINOIS

Chicago

Personal.—Dr. Joseph T. Meyer has received a Loyola University Alumni Citation, an engraved plaque, awarded to those whose "careers exemplify the ideals of Jesuit education." Dr. Meyer served in the Army Medical Corps, attaining the rank of captain, and after World War I he joined with his brothers, Dr. Raymond Meyer and the late Dr. Edwin Meyer, to establish a clinic on the south side. Dr. Meyer is president and chief surgeon of St. George Hospital.

New Chairman of Radiology Department.—Dr. Earl E. Barth, professor of radiology, Northwestern University Medical School, has been named chairman of the department of radiology, effective Sept. 1, to succeed Dr. Edward L. Jenkinson, who is retiring. Dr. Barth, a graduate of Northwestern Medical School, joined the faculty in 1931 as a fellow in radiology. In 1953 he was named a full professor. He is also chief consultant in radiology at the Veterans Administration Research Hospital, Chicago, a past-president of the Chicago Roentgen Society and a past-chairman of the executive council of the American Roentgen Ray Society, and now is chairman of the board of chancellors of the American College of Radiology.

Institute for Study of Congenital Heart Disease.—A Congenital Heart Institute sponsored by the Chicago Heart Association was started Sept. 1 and will continue for a minimum of 10 years. Dr. Maurice Lev has been hired as full-time investigator to devote all his time to a study of the life history and pathology of the defects of the heart. Dr. Lev will perform his investigative work in laboratory and working space provided for him in the Hektoen Institute of Chicago and the work will be done under the cooperation of the five Chicago medical schools, the Chicago Heart Center, and the health agencies of city and state. Dr. Lev plans to assemble clinical, laboratory, and pathologic data on cases of children who die of congenital heart defects. Cost of the institute will be about $50,000 a year.

Medical Associates of Chicago.—A medical facility, the Medical Associates of Chicago, has been organized by Dr. Nathaniel Calloway, professor of internal medicine, University of Illinois Medical School. This group, which has offices in the Lake Meadowbrook development, involves a collective investment of $700,000 and represents the first established group practice started by Negroes in the city with complete diagnostic facilities. The group has 14 physicians, three dentists, technicians, nurses, and office personnel, in all about 40 persons. The new offices house a pharmacy, medical diagnostic and dental laboratories. From 1951 to 1953, Dr. Calloway served as associate chief of medicine at Percy Jones Army Hospital, Battle Creek, Mich. He has served as a medical consultant to the U. S. public health service and the naval research project at the University of Illinois, and is a member of the Tuberculosis Institute of Chicago and Cook County.

KENTUCKY

State Medical Association Meeting.—The R. W. Gaines Memorial Meeting of the Kentucky State Medical Association will be held Sept. 16-19 at the Columbia Auditorium, Louisville. A panel discussion, "Hypothyroidism—Diagnosis and Management," will be moderated by Dr. Alton Ochsner, New Orleans, on Sept. 19. Color television sessions will include two symposiums: duodenal ulcer and congenital heart disease. The program includes the following topics by out-of-state speakers:

Tuberculosis in Childhood: Some Aspects of Prevention, Diagnosis and Treatment, Dr. Gardner Middlebrook, Denver.

Obstetrical Anesthesia and Analgesia, Dr. Ralph A. Reis, Chicago.

Pain as an Emotional Problem, Dr. Lawrence C. Kolb, New York City.

Role and Function of the National Eye Bank, Dr. Donald M. Shafer, New York City.

Modern Concepts in the Management of Hepatic Failure, Dr. John M. Rumball, Coral Gables, Fla.

Carcinoma of the Stomach, Dr. Alton Ochsner, New Orleans.

Preventable Errors in the Care of Orthopedic Injuries, Dr. Robert A. Knight, Memphis, Tenn.

Twelve specialty groups will present scientific programs simultaneously the afternoon of Sept. 18. Entertainment includes the President's Luncheon, at which Dr. Kenneth McFarland, Topeka, Kan., will speak on "Ropes of Gold." A special ladies' program is planned. For information write Mr. J. P. Sanford, 620 S. Third St., Louisville 2, Ky.

LOUISIANA

Graduate Medical Assembly.—The Southwest Louisiana Graduate Medical Assembly will hold its eleventh annual meeting at the Majestic Hotel, Lake Charles, Sept. 13-14. All physicians are invited to attend this meeting which is approved for category I by the American Academy of General Practice. The program includes the following topics by out-of-state speakers:

Outpatient Management of Hypertension, Dr. John Moyer, chairman, department of medicine, Hahnemann Medical College, Philadelphia.

Anxiety Heart Disease, Dr. Don Chapman, professor of medicine, Baylor University, Houston, Texas.

Common Duct Stone, Dr. Robert M. Moore, chairman, department of surgery, University of Texas, Medical Branch, Galveston.

The Interpretation of Chest Films in Pediatrics, Dr. Vincent P. Collins, professor of radiology, Baylor University College of Medicine.

The Practical Diagnosis of Bleeding Disorders, Dr. Jack Abbott, pathologist and director of laboratories, Methodist Hospital and Baylor University College of Medicine, Houston.

A panel discussion, "Diagnosis and Management of Thyroid Diseases," will be presented by Drs. Don Chapman, John Moyer, Jack Abbott, Vincent P. Collins, and Robert M. Moore. A clinico-pathologic conference and a round-table luncheon discussion also are scheduled. For information write Dr. Janie M. Topp, P. O. Box 568, Lake Charles 1, La.

MICHIGAN

Society News.—The following officers of the Michigan Allergy Society have been elected: Dr. Ernst O. Schreiber, Flint, president; Dr. Bernard Dickstein, Flint, vice-president; and Dr. Milton J. Steinhardt, Detroit, secretary-treasurer.

State Medical Society Meeting.—The 92nd annual session of the Michigan State Medical Society will be held Sept. 25-27 at the Pantlind Hotel, Grand Rapids. The annual presidential address will be given by Dr. Arch Walls, at the officers' night, after which Governor G. Mennen Williams will also present an address. The program includes special discussion conferences and the following panel discussions: Treatment of Polyps of the Rectum and Colon; The Problem of the Destructive Impulse in the Practice of Medicine; What's New in Heart Disease; and Patient-Centered Medical Care. The fifth Beaumont Lecture, "Cancer of the Lower Bowel: The Adenoma Carcinoma Sequence," will be presented by Dr. Raymond J. Jackman, head, section of proctology, Mayo Clinic, Rochester, Minn. Technical and scientific exhibits are scheduled. Entertainment includes the officers' night dinner-dance Sept. 25. Mr. Walter P. Reuther, Detroit, will speak on "Medicine and Labor in These Changing Times" the afternoon of Sept. 25. For information write Dr. L. F. Foster, 606 Townsend Street, Box 539, Lansing 15, Mich.

MISSOURI

Society News.—The following officers were elected by the members of the St. Louis Society of Anesthesiologists: president, Dr. Thomas Culkin; vice-president, Dr. Harry Sammons; secretary, Dr. Richard E. Hanna; and treasurer, Dr. Jean Merz.

Personal.—Dr. Walter J. Burdette professor of clinical surgery, St. Louis University School of Medicine, and director, St. Louis University Surgical Service at Veterans Hospital, has gone to Tokyo to visit medical and research institutions in Japan. One objective of the trip is in connection with the studies he has been conducting at the university on a hormone in relation to cancer. Following his stop in Japan Dr. Burdette will visit and lecture at medical and research centers in Thailand, India, Lebanon, Germany, France, Greece, and Turkey.——Dr. Norman Tobias, dermatologist of St. Louis, has returned from an extended trip to the Far East, where he lectured before the Tokyo, Bangkok, and Manila Medical Societies under the auspices of the World Medical Association.

NEBRASKA

General Practice Meeting in Omaha.—The annual meeting of the Nebraska Chapter of the American Academy of General Practice will be held Sept. 13-14 at the Fontenelle Hotel, Omaha. The presidential address will be given by Dr. Thomas D. Fitzgerald. A panel discussion with live television interviews on a closed-circuit direct from the Nebraska Psychiatric Institute on "Psychiatric Aspects of Surgical Practice" will be held on the morning of Sept. 13, with Dr. L. C. Strough serving as moderator. A luncheon program Sept. 13 includes addresses by Drs. Paul Read, president, Douglas County Medical Society; R. R. Best, president, Nebraska State Medical Society; and M. E. Phelps, president, American Academy of General Practice. Guest speaker at the banquet to be held the evening of Sept. 14 will be Dr. H. E. Campbell, Denver, member of the American Medical Association's Traffic Committee, whose topic is "Safety on Our Highways." A special ladies' program is planned. For information write Dr. C. R. Brott, Chairman, Program Committee, 2124 Elk St., Beatrice, Neb.

NORTH CAROLINA

Grant for Pituitary Study.—A grant of $31,050 from the U. S. Public Health Service has been made to Dr. Gordon Dugger, assistant professor of surgery, University of North Carolina School of Medicine, Chapel Hill, to be used for the study of the effects of pituitary gland operations on patients with cancer. Associated with Dr. Dugger in the research are Drs. James Newsome and Judson Van Wyk. Dr. Dugger was trained in neurosurgery at the Montreal Neurological Institute of Montreal, Canada.

GENERAL

Pediatricians Meeting in Chicago.—The 26th annual meeting of the American Academy of Pediatricians will be held Oct. 5-10 at the Palmer House, Chicago. Two symposiums are scheduled for the general sessions: current developments in infant nutrition, and animals and diseases. Three panel discussions are also scheduled: problems of the hospitalized child, iatrogenic disease, and congenital metabolic disease. Round-table discussions will be held Oct. 7 and 8. The Mead Johnson award presentation "Steroid Biogenesis in the Adrenal Cortex of Man" and "Some

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Studies on the Biochemistry of Connective Tissue," will be given by Drs. Alfred M. Bongiovanni and Walter R. Eberlein, of Philadelphia, and Dr. Albert Dorfman, Chicago, respectively. The Borden award presentation will be given by Dr. Arild E. Hansen, Galveston, Texas, on "Essential Fatty Acids in Infant Nutrition." A special quiz session will be held Oct. 8 under the direction of Dr. Robert B. Lawson, Miami, Fla. Scientific and commercial exhibits will be shown. A ladies' program is planned. Entertainment includes the annual banquet. For information write the Executive Officer, American Academy of Pediatricians, 1801 Hinman Ave., Evanston, Ill.

International Postgraduate Medical Association Meeting.—The 42nd International Scientific Assembly of the Interstate Postgraduate Medical Association will be held Sept. 30-Oct. 3 at the Palmer House, Chicago. Forty papers are scheduled for presentation. Three symposiums will be held on the following topics: what's new in obstetrics, surgery, and steroids; trauma; and the proper selection of cases for heart surgery. The following presentations will be made by Canadian speakers:

Abnormal Vaginal Bleeding in the Menopause, Dr. Newell Philpott, professor of obstetrics and gynecology, McGill University Faculty of Medicine, Montreal, Canada.

Clinical Management of the Allergic States, with Special Reference to Long-Term Steroid Therapy, Dr. Bram Rose, professor of medicine, McGill University Faculty of Medicine, Montreal.

A Neuro-Surgeon Looks at "Strokes," Dr. E. Henry Botterell, associate professor of surgery, University of Toronto, Canada.

The guest speaker at the annual dinner will be Kenneth McFarland, Ph.D., Topeka, Kansas, whose topic will be "Ropes of Gold." For information write Interstate Postgraduate Medical Association, Box 1109, Madison 1, Wis.

Radiological Research Awards.—The James Picker Foundation has announced two awards in the field of radiological research, in addition to those made public in June. As a part of its efforts in advancing the science of radiology, the foundation supports research grants, fellowships, and grants for scholars. These awards are made on recommendation of the National Academy of Sciences–National Research Council.

A research grant has been made to the University of Saskatchewan, Saskatoon, Canada, to permit continuation for a third year of Dr. Sidney P. Traub's studies on x-ray changes produced by increased pressure from within the skull. Dr. Traub is assistant professor of diagnostic radiology at the university College of Medicine.

The reappointment of Dr. Hans Ludin, of New York City, as a James Picker Foundation Fellow in Radiological Research is also announced. Under his fellowship, which began in 1956, Dr. Ludin has been studying the use of special techniques to visualize the pancreas on x-ray examination. This work is being carried out in the department of radiology, New York Hospital, New York City, under the guidance of Dr. John A. Evans.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	Aug. 10, 1957 Paralytic Type	Aug. 10, 1957 Total Cases	Aug. 11, 1956 Total Cases
New England States			
Maine	..	..	1
New Hampshire	..	1	1
Vermont	..	..	1
Massachusetts	..	1	11
Rhode Island	..	..	1
Connecticut	..	..	7
Middle Atlantic States			
New York	2	7	39
New Jersey	1	5	14
Pennsylvania	..	2	3
East North Central States			
Ohio	6	30	34
Indiana	..	8	25
Illinois	7	25	218
Michigan	4	40	32
Wisconsin	1	28	19
West North Central States			
Minnesota	1	6	5
Iowa	..	6	42
Missouri	..	10	24
North Dakota	1	2	..
South Dakota	3	18	3
Nebraska	1	3	12
Kansas	..	6	8
South Atlantic States			
Delaware	..	2	2
Maryland	1	1	..
District of Columbia	1	1	1
Virginia	4	4	13
West Virginia	..	1	10
North Carolina	1	25	24
South Carolina	1	6	6
Georgia	4	4	14
Florida	1	8	18
East South Central States			
Kentucky	4	6	7
Tennessee	2	6	6
Alabama	..	2	3
Mississippi	..	3	21
West South Central States			
Arkansas	2	4	12
Louisiana	2	9	41
Oklahoma	1	7	15
Texas	7	20	34
Mountain States			
Montana	..	1	1
Idaho	1	3	2
Wyoming	..	..	1
Colorado	1	3	5
New Mexico	1	5	4
Arizona	1	3	5
Utah	..	..	25
Nevada	..	..	3
Pacific States			
Washington	..	..	7
Oregon	1	1	9
California	7	33	87
Territories and Possessions			
Alaska	..	..	..
Hawaii	..	..	2
Puerto Rico	3	3	..
Total	73	359	878

Society News.—The following officers of the **American College of Physicians** have been installed: president, Dr. Richard A. Kern, Philadelphia; president-elect, Dr. Dwight L. Wilbur, San Francisco; first vice-president, Dr. Herbert K. Detweiler, Toronto; second vice-president, Dr. Charles A. Doan, Columbus, Ohio; third vice-president, Dr. Lemuel C. McGee, Wilmington, Del.——The newly elected officers of the **World Federation of Neurosurgical Societies** are: Dr. Paul C. Bucy, Chicago, president; Dr. E. Harry Botterell, Toronto, Canada, vice-president; Dr. Bronson S. Ray, New York, secretary-general; Dr. William B. Scoville, Hartford, Conn., assistant secretary-general; Dr. Barnes Woodhall, Durham, N. C., treasurer; Dr. Wallace B. Hamby, Buffalo, N. Y., assistant treasurer; and Dr. David L. Reeves, Santa Barbara, Calif., editor of the transactions. Dr. Percival Bailey, of Chicago, Dr. Wilder Penfield, of Montreal, Canada, Dr. H. Olivecrona, of Stockholm, Sweden, Dr. Paul Martin, of Brussels, Belgium, Dr. D. Petit-dutaillis, of Paris, France, and Sir Geoffrey Jefferson, of Manchester, England, are honorary presidents.——At the 67th annual meeting of the **American Pediatric Society** the following officers were elected for 1958: president, Dr. A. Ashley Weech, Cincinnati; vice-president, Dr. Alton Goldbloom, Montreal, Canada; secretary-treasurer, Dr. Aims C. McGuinness, Washington, D. C.; recorder-editor, Dr. Stewart H. Clifford, Brookline, Mass.—— The following officers of the **Pacific Northwest Society of Plastic and Reconstructive Surgery** have been installed: Dr. Ernest E. Banfield, Tacoma, president; Dr. Carl E. Chism, Seattle, president-elect; Dr. Verner V. Lindgren, Portland, vice-president, and Dr. Willard D. Rowland, Portland, secretary-treasurer.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part I.* Various Centers, Sept. 3-4. Sec., Dr. John B. Hubbard, 133 South 36th St., Philadelphia 4.

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Washington, Oct. 28-Nov. 1. Various locations in the United States and Canada, July 18. Final date for filing application is Jan. 18. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St. Hartford 15.

AMERICAN BOARD OF DERMATOLOGY: *Oral.* Baltimore, Oct. 11-13. Final date for filing application was April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 21. *Oral.* Los Angeles, Sept. 11-14. Final date for filing applications was Feb. 1. Exec. Sec., Dr. W. A. Werrell, 1 West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part I.* Chicago, Jan. 2. *Part II.* Chicago, May 7-17. Final date for filing application is September 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Chicago, Oct. 7-11. *Written.* January 1958. Final date for filing application was July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland 9, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Parts I and II, New York City, Jan. 29-31, 1958. Final date for filing application is August 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARNGOLOGY: Chicago, Oct. 7-11. Final date for filing application was in April. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written. Pathologic Anatomy and Clinical Pathology.* New Orleans, Sept. 26-28. Final date for filing application is August 15. Sec., Dr. Edward B. Smith, Indiana University Medical Center, Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 11-13. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written Examination.* San Francisco, Oct. 31-Nov. 2. Final date for filing case reports was July 1. Corresponding Sec., Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *In Public Health. Oral and Written.* Cleveland, Nov. 7-9. Sec., Dr. Thomas F. Whayne, 3438 Walnut St., Philadelphia.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written. Parts I and II.* September. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, Dec. 16-17. San Francisco, March 17-18. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S. W., Rochester Minn.

AMERICAN BOARD OF RADIOLOGY: Washington, Sept. 23-28. Final date for filing application was June 1. Chicago, May 20-24. Final date for filing application is Jan. 1, 1958. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part II.* Buffalo, Sept. 23-24; New Haven, Oct. 21-23; Indianapolis, Nov. 18-19; Cincinnati, Dec. 16-17; New Orleans, Jan. 13-14; Durham, N. Car., Feb. 10-11; Baltimore, March 10-11; Chicago, May 12-13; Los Angeles, June 16-17 and Portland, Oregon, June 20-21. Sec., Dr. John B. Flick, 225 So. 15th St., Philadelphia 2.

AMERICAN BOARD OF UROLOGY: *Written examination.* Various cities throughout the country. *Pathology and Oral Clinical.* February 1958. Location not decided. Exec. Secretary, Mrs. Ruby L. Griggs, 30 Westwood Road, Minneapolis 16.

BOARD OF THORACIC SURGERY: *Written.* Various centers throughout the country, Sept. 6, and the closing date for registration was July 1, 1957. Sec., Dr. William H. Tuttle, 1151 Taylor Ave., Detroit 2.

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GOVERNMENT SERVICES

AIR FORCE

Consultants Visit Medical Installations.—The following four consultants to the surgeon general recently visited Air Force medical installations in Europe, the Far East, and Alaska. They rendered services on problem cases in their specialties and conducted lectures and teaching sessions at various medical installations.

Dr. Francis M. Forster, dean, Georgetown University School of Medicine, and consulant in neurology, visited installations in England, France, Germany, Morocco, and Libya.

Dr. Jasper Lamar Callaway, professor of dermatology and syphilology, Duke University School of Medicine, and consultant in dermatology, visited installations in Japan, Korea, Okinawa, the Philippine Islands, and Taiwan.

Dr. Sidney S. Chipman, professor of maternal and child health, University of North Carolina School of Public Health, and consultant in pediatrics, and Dr. Marvin E. Chapin, professor of oral surgery, University of North Carolina, and consultant in oral surgery, both visited installations in Alaska.

Personal.—At the School of Aviation Medicine in Texas, Dr. Lawrence E. Lamb has been appointed chief of the department of internal medicine. Dr. Lamb did research in Switzerland in 1954 on electrocardiography as a fellow of the American Heart Association. He is the author of a forthcoming book, "Fundamentals of Electrocardiography and Vectorcardiography."

Conduct Awards Made.—The following Air Force medical officers have been awarded the Legion of Merit for exceptionally meritorious conduct in the performance of outstanding service: Col. Manah R. Halbouty, commander, 3605th U. S. A. F. Hospital, Ellington Air Force Base, Texas; Col. Robert A. Patterson, surgeon, Eastern Air Defense Force, Stewart Air Force Base, New York; Col. Philip P. Pease, commander, 7272nd U. S. A. F. Hospital, Wheelus Air Force Base, Libya.

ARMY

Wings for Army Aviation Medical Officers.—First award of silver Army aviation wings to 50 Army Medical Corps officers marks the newest development in the Army aviation medicine program according to Major Gen. Silas B. Hays, surgeon general of the Army. The new badge has the caduceus superimposed on the shield of the Seal of the United States centering the wings.

Officers designated to wear these wings already have non-crew-member flying status and pay, and they also perform clinical duties for non-flying personnel. They are officially recognized as being qualified to conduct medical examinations for flying, to exercise supervision over the health of flying personnel, and to furnish medical advice related to Army aviation. They receive their aviation medical training at the Air Force School of Aviation Medicine, Randolph Air Force Base, Texas, or at the Navy School of Aviation Medicine, Pensacola, Fla. On completion of either of these courses, the Army graduates are sent to the Army Aviation School, Fort Rucker, Ala., for applicatory instruction in Army aviation medical practice.

The 50 medical officers awaiting their wings are to be found with infantry, armored, and airborne divisions, with station medical complements responsible for the care of significant concentrations of Army aviators, and with a variety of special Army aviation activities. They are stationed in Germany, Japan, Korea, the Territory of Hawaii, and the Canal Zone. They are serving at installations across the United States from Fort Lewis, Wash., to Fort Benning, Ga., from the Army Medical Research Laboratory, Fort Knox, Ky., to the Walter Reed Army Medical Center.

Personal.—Col. Joseph P. Russell has been named Post Surgeon and Commanding Officer of the Army Hospital at Fort Leavenworth, Kan., succeeding Col. Norman Anderson.

VETERANS ADMINISTRATION

Study of Sarcoidosis.—The project sponsored by the Veterans Administration to investigate the etiology of sarcoidosis will be carried on in five hospitals which will contribute information on the environment, occupation, eating habits, and self-medication of patients affected by this disease. The central office research team is composed of Dr. Martin M. Cummings, director of research service; Dr. Edward Dunner, secretary of the Veterans Administration–armed forces committee on chemotherapy of tuberculosis; Dr. Richard H. Schmidt Jr., tuberculosis service; and J. H. Williams of research statistics. Seventeen hundred cases of sarcoidosis were diagnosed in these hospitals between the years 1949 and 1956.

Personal.—Dr. Thomas J. Ready, director, professional services, VA Hospital, Providence, R. I., was transferred as manager of the VA Hospital at Washington, D. C., to fill the vacancy created by the retirement of Dr. Edwin J. Rose on June 30.——Dr. Kenneth W. Brown, director, professional services, VA Hospital, Omaha, has been appointed to the combined position of manager and director of professional services at the VA Hospital, Clarksburg, W. Va., to fill the vacancy created by the retirement of Dr. Louis M. Hohman on June 26.——Dr. Abraham M. Kleinman, director of professional services, VA Hospital, Brooklyn, N. Y., has been appointed manager of the VA Hospital in the Bronx, New York City, a 1,372-bed general medical and surgical facility.——Dr. Richard B. Bean, area director of professional services, VA Area Medical Office, Boston, had become manager of

the VA Hospital at Boston, replacing Dr. George P. Denny who retired June 30, 1957. The hospital is a 920-bed general medical and surgical facility.

Mental Hospital as a Therapeutic Community.—The Veterans Administration is trying to develop the mental hospital into a therapeutic community that will prepare recovering patients for the life they will lead outside the hospital. A pilot program is under way at the VA Hospital in St. Cloud, Minn.

Dr. Jesse F. Casey, VA director of psychiatry and neurology, said the nub of the St. Cloud program is a "motivation unit," directed by Dr. W. R. Coutant. This unit consists of a ward with 80 patients selected from the entire hospital and a foster home program under which 55 patients live outside the hospital on a trial basis. Patients living in the ward are encouraged to become friends, to work at jobs in the hospital, to attend recreational activities together, and to live much as they would outside the hospital. Once a week they gather in groups of 10 to talk about their feelings and fears of returning to the community, Dr. Casey said, and efforts are made by the staff to allay the fears and build up the patients' trust and confidence. When the ward patients are ready, they are placed with families in the St. Cloud area.

Only about 10% of those in foster homes have returned for further hospitalization, and in the two years since the motivation unit was established the number of discharges from the hospital has risen from less than 300 a year to about 600. The staff of the unit includes also a social worker, a psychiatric nurse, a clinical psychologist, and the hospital's vocational counselor.

Former Long-term Patients Now at Work.—Increasing numbers of long term patients are able to leave VA hospitals to take paying jobs under a new vocational guidance program. During the first three months of 1957, a total of 2,825 patients were placed in jobs outside the hospital by the VA's vocational counseling service and through state and local agencies. The figure includes veterans who have recovered from mental illness, tuberculosis, and other seriously disabling illnesses.

Study of Fungus Pulmonary Diseases.—Comprehensive studies of two lung diseases (histoplasmosis and coccidioidomycosis), which simulate tuberculosis, have been started by the VA in cooperation with the Armed Forces, the VA announced July 23. The studies are aimed at testing the effectiveness of new drugs which show promise in treatment.

Tentative case registries of some 500 patients with histoplasmosis or coccidioidomycosis in VA hospitals during the past two years have been established for study. Diagnoses are being substantiated by laboratory tests.

The histoplasmosis study is being carried out at seven VA hospitals, and at the Naval Hospital, St. Albans, N. Y., and Fitzsimons Army Hospital, Denver.

Central laboratories for the study have been established at the Kennedy Division of the VA's Memphis Hospital, and at Walter Reed Army Hospital in Washington, D. C.

Fourteen VA and Armed Forces hospitals are making the study of coccidioidomycosis. The central laboratory for the coccidioidomycosis study is at the VA's San Fernando, Calif., Hospital.

PUBLIC HEALTH SERVICE

Program to Encourage Research on Aging.—A new research approach to the health problems of older persons was launched on Aug. 1, as Surgeon General Leroy Burney announced a $306,922 award to Duke University in a special ceremony on the university campus at Durham, N. C. The award is the first grant in the Public Health Service's new program to encourage establishment of research centers in which many departments of a university, and the health and related agencies of a community will cooperate in studying various aspects of aging.

The program at Duke University has four main objectives: (1) To develop a Center for Aging Research based on a university-wide effort. (2) To support fundamental research concerned with health problems of aging and to include relevant research contributions from the social and behavioral sciences and related fields. (3) To train investigators interested in the problems of aging. (4) To foster a regional resource for the dissemination of scientific knowledge in the field of aging.

The Public Health Service program to encourage such research is sponsored by the Center for Research on Aging at the National Institutes of Health, Bethesda, Md., established in October, 1956, under the direction of Dr. G. Halsey Hunt.

Research on Cerebral Vascular Disease.—The launching of a nationwide cooperative research program on cerebral vascular disease has been announced by the surgeon general. Ten medical research centers in nine states have already joined in the program, and it is expected that many more institutions will ultimately participate. The program, which is expected to run several years, is under the auspices of the National Institute of Neurological Diseases and Blindness of the National Institutes of Health. The program was made possible by grants to the participating organizations, recommended by the National Advisory Neurological Diseases and Blindness Council. The program is concerned specifically with patients suffering from cerebral vascular disease involving hemorrhage, blood clots, aneurysms, and malformations of the arteries or veins of the brain. It has been estimated that as many as 1,800,000 living Americans have suffered cerebral strokes at one time or another and that deaths due to such strokes number about 175,000 annually. This research is expected to shed new light on the nature and causes of strokes and to open the way to more effective treatment.

DEATHS

Moorhead, John Joseph, Millbrook, N. Y.; born in New York City July 15, 1874; New York University Medical College, New York City, 1897; professor emeritus of surgery at the New York University Post-Graduate Medical School in New York City; an associate member of the American Medical Association; member of the American Association for the Surgery of Trauma; fellow of the American College of Surgeons; member of the founders group of the American Board of Surgery; decorated for his service in France in World War I; received the Croix de Guerre and the Cross of the Legion of Honor; his own country awarded him the Gold Medal of Honor, the Distinguished Service Cross, and the Distinguished Service Medal; presented with a medal by the Honolulu County (Hawaii) Medical Society for helping care for the wounded following the Japanese attack on Pearl Harbor Dec. 7, 1941, when he was in Honolulu as the guest of the society; in 1944 retired as medical director of the New York City Transit Company; consultant, New York Post-Graduate Medical School and Hospital, Mother Cabrini Memorial and Harlem hospitals in New York City, Yonkers (N. Y.) General Hospital, Nyack (N. Y.) Hospital, Caledonian Hospital, Brooklyn, New Rochelle (N. Y.) Hospital, Mary Immaculate Hospital, Jamaica, Rockland State Hospital in Orangeburg, Rahway (N. J.) Hospital, Fitkin Memorial Hospital, Neptune, N. J., and the All Souls Hospital, Morristown, N. J.; in 1941 received the honorary degree of doctor of science from New York University; author of "Clinical Traumatic Surgery"; died July 1, aged 82, of acute dilatation of the heart.

Larsen, Reuben Leonard, Lieut. Commander, U. S. Navy, retired, Seattle; born on Jan. 25, 1890; Northwestern University Medical School, Chicago, 1916; service member of the American Medical Association; veteran of World War I; commissioned in the regular Navy in 1917; placed on the retired list November, 1920, due to physical disability; at the outbreak of World War II requested recall to active duty and on Dec. 26, 1941, reported to the Naval Air Station, Corpus Christi, Texas, for active duty; released to inactive duty on Oct. 20, 1945; during his more than seven years active service, served with Naval medical department facilities throughout the United States and abroad and in ships of the fleet; died in the U. S. Naval Hospital, Bremerton, June 21, aged 67, of hemopericardium and myocardial infarction.

Comfort, Charles Williams Jr. ✦ New Haven, Conn.; born in Philadelphia in 1885; Yale University School of Medicine, New Haven, 1911; served in World War I, and was awarded the Distinguished Service Cross and the French Croix de Guerre; during World War II was division surgeon and commanded the 118th Medical Regiment of the 43rd division, National Guard; retired with the rank of colonel in 1946; formerly secretary of the Connecticut State Medical Society; member of the city welfare board; on the staff of the Grace-New Haven Community Hospital; died in the Veterans Administration Hospital, Rocky Hill, May 6, aged 71, of coronary thrombosis.

Higgins, William Harrison ✦ Richmond, Va.; born in Stanford, Ky., in 1883; Johns Hopkins University School of Medicine, Baltimore, 1908; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the American Clinical and Climatological Association; past-president of the Richmond Heart Association, Richmond Academy of Medicine, and the Richmond Board of Health; formerly on the faculty of the Medical College of Virginia; on the staff of the Medical College of Virginia, Hospital Division; consultant, St. Elizabeth's Hospital; died June 8, aged 73, of cerebral hemorrhage.

Jesberg, Simon, Los Angeles; born in Franklin, Iowa, Sept. 16, 1886; College of Physicians and Surgeons, Los Angeles, 1913; an associate member of the American Medical Association; member of the American Broncho-Esophagological Association; member and formerly vice-president of the American Laryngological, Rhinological and Otological Society; specialist certified by the American Board of Otolaryngology; formerly on the faculty of the University of Southern California School of Medicine; served in France during World War I; associated with the Eye and Ear Hospital; died June 24, aged 70, of cerebral hemorrhage.

Alley, Ralph Martin ✦ Orofino, Idaho; born in Benwood, W. Va., Feb. 9, 1901; Jefferson Medical College of Philadelphia, 1927; member of the American College of Chest Physicians and the American Trudeau Society; veteran of World War II; at one time associated with the Indian Service; served as superintendent of the State Tuberculosis Sanatorium in Socorro, N. M., and the Shawnee (Okla.) Indian Sanatorium, and as chief of the student health service, University of Idaho in Moscow; on the staff of the State Hospital, where he died May 10, aged 56, of coronary occlusion.

Christenberry, Henry Eddie ✦ Knoxville, Tenn.; born in Oliver Springs, Tenn., Sept. 12, 1884; University of Tennessee Medical Department, Nashville, 1907; specialist certified by the American Board of Otolaryngolo-

✦ Indicates Member of the American Medical Association.

gy; fellow of the International College of Surgeons; served as member and chairman of the city school board; at one time mayor of Lonsdale; the Christenberry Junior High was named for him; on the staff of the Knoxville General Hospital; medical director and owner of Dr. H. E. Christenberry Eye, Ear, Nose and Throat Infirmary; died in the East Tennessee Baptist Hospital May 20, aged 72.

Mellen, Richard Hager ✦ Colorado Springs, Colo.; born in Middlebury, Vt., Oct. 23, 1909; Harvard Medical School, Boston, 1935; certified by the National Board of Medical Examiners; specialist certified by the American Board of Orthopedic Surgery; member of the Clinical Orthopaedic Society, American Academy of Orthopaedic Surgeons, and the American Society for Surgery of the Hand; veteran of World War II; chief of staff, Glockner Penrose Hospital; on the staffs of the Memorial and St. Francis hospitals; died June 8, aged 47, of coronary occlusion and myocardial infarction.

Robertson, Roy Lamar ✦ Monroe, La.; born in Rayville, La., Dec. 14, 1918; Emory University School of Medicine, Atlanta, 1942; interned at the Peter Bent Brigham Hospital in Boston; served a residency at the Grady Memorial Hospital in Atlanta, Ga.; formerly on the faculty of the Emory University School of Medicine in Atlanta; specialist certified by the American Board of Surgery; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; veteran of World War II; on the staffs of the E. A. Conway Memorial and St. Francis hospitals; died in Shreveport May 29, aged 38.

Copeland, N. Newall, Pittsfield, Mass.; born in 1896; McGill University Faculty of Medicine, Montreal, Quebec, Canada, 1922; member of the Massachusetts Medical Society; fellow of the American College of Surgeons; chief of surgical staff of Pittsfield General Hospital; an associate surgeon at St. Luke's and Hillcrest hospitals; veteran of the Canadian Army during World War I; past-president of the Berkshire District Medical Society and the Pittsfield Surgical Club; vice-president of the Union Federal Savings and Loan Association; died May 22, aged 60.

Hill, Robert Henry ✦ Newark, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1926; fellow of the American College of Surgeons; specialist certified by the American Board of Surgery; on the staffs of the Presbyterian Hospital and the Harrison S. Martland Medical Center; on the courtesy staffs, Hospital of St. Barnabas and for Women and Children, St. James and St. Michael's hospitals and Babies Hospital–Coit Memorial; consultant, Newark Eye and Ear Infirmary; died June 24, aged 63, of coronary arteriosclerosis.

Beebe, Linn Clair, Hamilton, N. Y.; Baltimore Medical College, 1895; veteran of World War I; during World War II a member of the County Medical Committee for Procurement and Assignment; served as county coroner, postmaster, health officer, and head of the department of health, Colgate University; died in the Community Memorial Hospital June 12, aged 83, of hiccoughs of three weeks duration, associated with esophageal hernia and diverticulum of the terminal part of the esophagus.

Blair, William W., Pittsburgh; Hahnemann Medical College and Hospital of Philadelphia, 1889; professor emeritus of ophthalmology at the University of Pittsburgh School of Medicine; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; associated with the Eye and Ear Hospital and St. Margaret Memorial Hospital; died June 12, aged 90, of heart disease.

Bliss, Guy Luvergne, Claremont, Calif.; Rush Medical College, Chicago, 1908; an associate member of the American Medical Association; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; fellow of the American College of Physicians; formerly practiced in Long Beach, where he was associated with the Seaside Memorial, Long Beach Community, and St. Mary's Long Beach hospitals; died June 2, aged 79, of coronary disease.

Simon, Arthur R. ✦ Sarasota, Fla.; Indiana University School of Medicine, Indianapolis, 1908; member of the Radiological Society of North America and the Indiana State Medical Society; specialist certified by the American Board of Radiology; formerly practiced in La Porte, Ind., where he was on the staffs of the Holy Family Hospital and the Fairview Hospital; died in the Memorial Hospital May 1, aged 70, of rupture of dissecting aneurism of the superior mesenteric artery.

Ahlbrandt, Charles G. C., Kirkwood, Mo.; Missouri Medical College, St. Louis, 1895; died June 20, aged 81.

Alford, Leland Barton ✦ St. Louis; Washington University School of Medicine, St. Louis, 1912; associate professor of neurology and psychiatry at St. Louis University School of Medicine; served on the faculty of his alma mater; member of the American Psychiatric Association; veteran of World War I; associated with St. Mary's Group of Hospitals, St. Louis City Hospital, and the Barnes Hospital, where he died May 14, aged 71, of acute myocardial infarction.

Ames, George Chester ✦ Hollis, N. Y.; University and Bellevue Hospital Medical College, New York City, 1924; on the staff of the Mary Immaculate Hospital, Jamaica; died in Amityville May 11, aged 62, of coronary thrombosis.

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Anderson, Edgar Walker ✱ Conroe, Texas; University of Arkansas School of Medicine, Little Rock, 1928; died in the Methodist Hospital, Houston, May 11, aged 55.

Anderson, Walter Marius ✱ Lompoc, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1929; member of the American Academy of General Practice; specialist certified by the American Board of Internal Medicine; on the staffs of the Santa Barbara (Calif.) Cottage Hospital and the Lompoc Hospital; died April 10, aged 53, of coronary disease.

Angus, Catherine Isabel, New York City; University of Wisconsin Medical School, Madison, 1934; on the staff of the St. Luke's Hospital; for many years physician in the Long Lines Department of the American Telephone and Telegraph Company; died in the University Hospital June 17, aged 48.

Arne, James A., Marion, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1922; member of the Massachusetts Medical Society; on the staff of the Lawrence Memorial Hospital in Medford; died in the Tobey Hospital, Wareham, May 5, aged 61, of coronary occlusion.

Ashworth, Robert Fraser ✱ Eclectic, Ala.; Hospital College of Medicine, Louisville, Ky., 1903; veteran of World War I; member of the American Urological Association; died in East Tallassee May 8, aged 74, of cerebral hemorrhage, arteriosclerosis and chronic myocarditis.

Babcock, Jay Blaine, Los Angeles; University of Nebraska College of Medicine, Omaha, 1925; veteran of World War I; at one time superintendent of the Hastings (Neb.) State Hospital; died May 25, aged 59, of peritonitis and cholecystitis.

Baber, James H., Huntington, W. Va.; University of Louisville (Ky.) Medical Department, 1895; an associate member of the American Medical Association; died June 11, aged 82.

Barcroft, John Woolverton, Waldport, Ore.; University of Oregon Medical School, Portland, 1919; also a graduate in pharmacy; died May 13, aged 68, of arteriosclerotic heart disease.

Barnwell, Columbus Hershel ✱ Chattanooga, Tenn.; Northwestern University Medical School, Chicago, 1933; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; veteran of World War II; associated with the Baroness Erlanger and Memorial hospitals; accidentally drowned in a pond on his farm on Little Sand Mountain near Summerville, Ga., June 2, aged 52.

Bass, Farris Euestus, Lebanon, Tenn.; Meharry Medical College, Nashville, 1924; a veteran of World War I; died June 10, aged 65, of hypertension.

Beatty, Ernest Nutter ✱ Santa Barbara, Calif.; University of Cincinnati College of Medicine, 1920; member of the Ohio State Medical Association; formerly practiced in Cincinnati, where he served as president of the Cincinnati Obstetrical Society and as a member of the staffs of St. Francis and Deaconess hospitals; died in Louisville, Ky., June 8, aged 62.

Beck, Henry Walter ✱ Gray, Maine; University of Vermont College of Medicine, Burlington, 1927; veteran of World War I; on the courtesy staffs of the Central Maine General Hospital, Lewiston, and the Mercy Hospital and Maine Eye and Ear Infirmary in Portland; served two terms on the school board; died June 4, aged 63, of cancer of the liver.

Becker, Morris R., Cambridge, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1933; died June 10, aged 50.

Beckman, George Edwin ✱ Jacksonville, Fla.; Medical College of South Carolina, Charleston, 1909; specialist certified by the American Board of Anesthesiology; died in St. Vincent's Hospital March 27, aged 77, of cerebral hemorrhage, hypertension and chronic interstitial nephritis.

Benson, Iver Simeon, Portland, Ore.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; died May 23, aged 75.

Berrey, Ivan Columbus ✱ Birmingham, Ala.; Rush Medical College, Chicago, 1927; served on the faculty of Medical College of Alabama; on the staffs of the University and Baptist hospitals; died April 26, aged 58, of carcinoma of the pancreas.

Bickel, John Edward ✱ Fort Wayne, Ind.; Medical College of Indiana, Indianapolis, 1897; member of the staff, St. Joseph's Hospital, where he died June 23, aged 83, of coronary thrombosis and myocardial infarction.

Blair, Ezekiel Slaughter ✱ Gadsden, Ala.; University of Nashville (Tenn.) Medical Department, 1910; died May 28, aged 76, of bronchopneumonia.

Bockhorst, Arthur L., Milwaukee; Kansas City (Mo.) Medical College, 1899; died in the Milwaukee County Hospital June 24, aged 82, of diabetes mellitus.

Boddie, Julian Franklin, Milledgeville, Ga.; Meharry Medical College, Nashville, Tenn., 1913; associated with the Baldwin County Hospital, where he died June 18, aged 66, of cerebral hemorrhage.

Bondar, H. Kelliher, Brooklyn; McGill University Faculty of Medicine, Montreal, Quebec, Canada, 1932; member of the American Psychiatric Association; specialist certified by the American Board of Psychiatry and Neurology; associated with the Cumberland and St. John's Episcopal hospitals; died in the Queens General Hospital, Jamaica, May 25, aged 49.

Brady, Rolland Roy * Ainsworth, Neb.; University of Nebraska College of Medicine, Omaha, 1931; member of the American Academy of General Practice; on the staff of the Ainsworth Clinic and Hospital; died in Omaha June 28, aged 53.

Brady, Richard Randall, Miles City, Mont.; University of Nebraska College of Medicine, Omaha, 1925; lieutenant colonel in the medical corps, Army of the United States; surgeon of the U. S. Army's Neurnberg, Germany, sub-area; died in Berchtesgaden, Germany, May 1, aged 56, of coronary disease.

Breslin, Robert Henry, Warwick, R. I.; College of Physicians and Surgeons, Baltimore, 1915; member of the Rhode Island Medical Society; veteran of World War I; on the staffs of the Roger Williams General Hospital and St. Joseph's Hospital, where he died June 25, aged 68.

Bruninghaus, Charles Walter, Worcester, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1915; veteran of World War I; died May 29, aged 76, of coronary artery disease.

Burnes, Eugene Howard, Rochester, N. Y.; Albany Medical College, 1908; an associate member of the American Medical Association; member of the American Academy of General Practice; past-president of the Rochester Pathological Society; veteran of World War I; during World War II chairman of Draft Board number 550; served on the staffs of St. Mary's Hospital and the Highland Hospital, where he died May 20, aged 72, of acute cardiac dilatation.

Burt, Elmer Gordon * Magnolia, Ark.; University of Arkansas School of Medicine, Little Rock, 1932; member of the American Academy of General Practice; veteran of World War II; died in the City Hospital April 26, aged 49, of a heart attack.

Butler, John Culbertson * Laurel, Miss.; Memphis (Tenn.) Hospital Medical College, 1904; veteran of World War I; died in the Veterans Administration Center, Biloxi, May 8, aged 79, of emphysema.

Butzow, Theodore Frederick, San Diego, Calif.; Rush Medical College, Chicago, 1897; veteran of World War I; died in the Mercy Hospital May 31, aged 86, of fracture of the hip and pneumonia.

Chaffin, Emory Franklin * Toccoa, Ga.; Atlanta Medical College, 1914; died in the Hall County Hospital, Gainesville, May 21, aged 71, of a heart attack.

Chambers, Dorsey Perry, Stilwell, Okla.; Barnes Medical College, St. Louis, 1896; died in the City Hospital May 6, aged 84, of cerebral hemorrhage.

Child, Florence Chapman, Deerfield Beach, Fla.; Johns Hopkins University School of Medicine, Baltimore, 1909; died in the North Broward General Hospital, Fort Lauderdale, March 30, aged 71, of carcinoma of the breast with metastases.

Cohen, Emanuel Samuel * Redwood City, Calif.; Columbia University College of Physicians and Surgeons, New York City, 1943; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; served as assistant clinical professor of medicine at the University of California School of Medicine in San Francisco; veteran of World War II; on the staff of the Sequoia Hospital; died May 31, aged 37.

Clark, Carl George, Burlington, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1905; died in St. Francis Hospital April 17, aged 80, of cardiovascular renal disease.

Cleere, Reuel C., Danville, Ala.; Birmingham Medical College, 1909; died in the Bryce Hospital, Tuscaloosa, May 1, aged 72.

Conley, Byron Richard, Salyersville, Ky.; University of Louisville (Ky.) Medical Department, 1907; member of the Kentucky State Medical Association; died in Ashland May 3, aged 74, of nephritis.

Cooper, Thomas Logan * Logansport, Ind.; University of Pittsburgh School of Medicine, 1912; on the staffs of St. Joseph's Hospital and the Memorial Hospital, where he died May 20, aged 74.

Crawford, Lewis B., New Iberia, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1905; fellow of the American College of Surgeons; associated with the Iberia General Hospital, where he died May 17, aged 74.

Cretzmeyer, Charles Henry * Algona, Iowa; State University of Iowa College of Medicine, Iowa City, 1901; on the staff of St. Ann Hospital, where he died May 6, aged 78, of a heart attack.

Cummings, Claude Wiggins, Colonel, U. S. Army, retired, San Francisco; Vanderbilt University School of Medicine, Nashville, Tenn., 1912; service member of the American Medical Association; veteran of World War I; entered the medical corps of the U. S. Army in 1917; retired Sept. 30, 1944; died in the Letterman Army Hospital May 6, aged 76.

Finady, William Aaron, Bethlehem, Pa.; Medico-Chirurgical College of Philadelphia, 1910; member of the Medical Society of the State of Pennsylvania; fellow of the American College of Surgeons; on the staff of St. Luke's Hospital, where he died June 29, aged 69.

Garrison, Amos Rule, Bvington, Tenn.; University of Louisville (Ky.) Medical Department, 1904; past-president of the Knox County Medical Society; for many years member of the county school board; died in the Fort Sanders Presbyterian Hospital, Knoxville, June 26, aged 78.

Hall, Henry Francis, Chicago; Meharry Medical College, Nashville, Tenn., 1909; died in the Manteno (Ill.) State Hospital April 14, aged 80.

Hankins, Frances Cantrall, Alhambra, Calif.; Northwestern University Woman's Medical School, Chicago, 1893; died July 6, aged 96, of coronary heart disease.

Harrelson, Rose Cranse Jr., Tabor City, N. C.; Jefferson Medical College of Philadelphia, 1945; veteran of World War II; on the staff of the Loris (S. C.) Community Hospital; accidentally drowned in Myrtle Beach, S. C., June 27, aged 36.

Hatcher, Martin Armstead, Hamlet, N. C.; Medical College of Virginia, Richmond, 1918; member of the Medical Society of the State of North Carolina; past-president of the Richmond County Medical Society; member of the Richmond Selective Service Board; veteran of World War I; on the staff of the Richmond County Memorial Hospital, Rockingham, and the Hamlet Hospital; died June 23, aged 66.

Hennell, Herman * New York City; Long Island College Hospital, Brooklyn, 1920; member of the American Trudeau Society; served on the faculty of Columbia University College of Physicians and Surgeons; on the staff of the Mount Sinai Hospital; died July 1, aged 68, of coronary disease.

Holtzhausser, George J., Philadelphia; University of the South Medical Department, Sewanee, Tenn., 1899; also a graduate in pharmacy; an associate member of the American Medical Association; died June 30, aged 84.

Hutchinson, James Thomas * Lubbock, Texas; Tulane University School of Medicine, New Orleans, 1909; veteran of World War I; past-president of the Lubbock–Crosby Counties Medical Society; member of the board of trustees of the Lubbock Independent School District for a 35-year period, 33 of which were spent as board chairman; formerly director of the First National Bank of Lubbock; associated with the Methodist Hospital, where he died June 22, aged 76.

Jellis, Walter, Somerville, Mass.; Tufts College Medical School, Boston, 1920; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the Massachusetts Medical Society; veteran of World War II; died May 12, aged 59, of heart failure.

Kauffmann, Louis John * Millville, N. J.; Jefferson Medical College of Philadelphia, 1910; on the staff of the Millville Hospital, where he died June 24, aged 68.

Koskela, Albert Leo * Santa Cruz, Calif.; University of Minnesota Medical School, Minneapolis, 1946; member of the American Academy of General Practice; died July 2, aged 37.

Leary, Maurice Thomas * Meadville, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1917; on the staffs of the Meadville City Hospital and the Spencer Hospital, where he died June 27, aged 61, of heart disease and hypentension.

Leavitt, Harry Clayton, Long Beach, Calif.; Chicago Medical School, 1938; service member of the American Medical Association; member of the American Psychiatric Association; specialist certified by the American Board of Psychiatry and Neurology; veteran of World War II; associated with the Veterans Administration Hospital; died May 31, aged 45, of coronary thrombosis.

Leopold, Raymond Sylvester * Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1906; formerly executive vice-president and trustee, Hahnemann Medical College and Hospital; served on the state board of medical education and licensure; died in the Germantown Hospital June 30, aged 73.

Lesses, Max * Salem, Mass.; Queen's University Faculty of Medicine, Kingston, Ontario, Canada, 1905; on the staff of the J. B. Thomas Hospital in Peabody; formerly on the staff of the Union Hospital, Lynn; died in the Beth Israel Hospital, Boston, July 4, aged 75, of carcinoma of the pancreas.

Malley, George Calvert * Zanesville, Ohio; Long Island College of Medicine, Brooklyn, 1930; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; past-president of the Good Samaritan Hospital staff; served as chief of pediatrics at Bethesda Hospital; died June 12, aged 53.

Marks, Julian Barnett * Los Angeles; University of Illinois College of Medicine, Chicago, 1918; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; died in the Santa Monica (Calif.) Hospital April 5, aged 65, of coronary thrombosis.

Martin, Ruben Ferdinand, San Antonio, Texas; St. Louis University School of Medicine, 1910; veteran of World War I; died in the Veterans Administration Center, Temple, May 21, aged 72.

McFarland, George Edwin * Los Angeles; University of Minnesota Medical School, Minneapolis, 1942; veteran of World War II; at one time health officer of San Luis Obispo County; on the staff of the California Lutheran Hospital; died in the Centinela Valley Community Hospital, Inglewood, Calif., June 23, aged 45, of seminoma with metastasis.

Meharg, Shelton Theodore, Anniston, Ala.; Memphis (Tenn.) Hospital Medical College, 1900; during World War I served as acting assistant surgeon in the U. S. Public Health Service; served as director of Anniston National Bank; died June 19, aged 78.

Milligan, Edd Fitch * Geary, Okla.; Denver and Gross College of Medicine, Denver, 1905; veteran of World War I; died June 16, aged 81, of pneumonia.

Moore, Robert W., Memphis, Tenn.; Meharry Medical College, Nashville, 1914; died May 7, aged 71, of cerebral hemorrhage and hypertension.

FOREIGN LETTERS

AUSTRIA

Unusual Case of Pleurisy.—At the meeting of the Vienna Society of Physicians on June 21, A. Sattler reported the case of a 62-year-old physician who had had amebic dysentery in 1941. The patient fell seriously ill in December, 1956, with diarrhea, abdominal pains, and fever. Treatment with antibiotics was without result. The patient was admitted to the hospital where the diagnosis of sigmoiditis and diverticulitis and a hemorrhagic exudative pleurisy on the left was made. Thoracoscopy was requested because the patient's cachexia and the hemorrhagic exudate suggested cancer. The thoracoscopy was performed with difficulty because of the basal sacculation. Finally sufficient space for endoscopy was made by aspirating 300 cc. of exudate and replacing it with air. There was no evidence of pleurocarcinoma but rather of true pleurisy. The most remarkable findings were two cystoid formations of the dorsal part of the lungs, which were inflated at inspiration and retracted in a funnel-shaped form at expiration. A blood clot was observed on top of one of these formations. This finding ruled out a malignant exudation. The cystoid formations were believed to be residues of pulmonary abscesses. The cause of the disease could not be determined by inspection. Because of the patient's history of amebiasis, a parasitologist was called in and he was able to identify trophozoites of Entamoeba histolytica in the pleural fluid and rectal smears.

Chemotherapy of Malignant Tumors.—At the sixth Austrian Cancer Meeting held in Vienna in May, H. J. Wolf and N. Gerlich (Bielefeld) said that they had used ethyleneimine quinone (E-39) in treating 265 patients suffering from all kinds of malignant tumor. Only patients with inoperable tumors or with metastases were included in this series. Since it is important to have the cytostatic drug act on the tumor in a most concentrated form and as long as possible, the drug was injected directly into the tumor. A temporary disappearance of the tumor may thus be obtained and this without the formation of necrosis or abscess. Toxic manifestations are minimal when the drug is used in this way, but if it is given intravenously, not only is proliferation inhibited in the tissue of the tumor but also the formation of leukocytes, erythrocytes, and thrombocytes in the marrow and reproductive cells in the gonads is inhibited, and growth in children may be hindered. It appears, therefore, important to give large doses for a short time and to repeat the treatment at intervals after the restoration of the leukocytes.

E. Bauer (Vienna) said that in using E-39 it is important that this treatment be given at the optimum time. Autointoxication can be prevented by the removal of the already necrotic tumor masses. This relieves the pain of tension and produces an improvement of the general condition. The leukocyte count is not a reliable guide to dosage. The bone-marrow inhibitory effect of the drug and the leukocytosis stimulated by the necrotic tumor act antagonistically. A complete withdrawal of the drug or special therapeutic measures were never necessary, not even in patients with a marked leukopenia. Treatment with E-39 must be given intravenously for a long period (the exact duration is still undetermined), if one does not want to risk a widespread metastasis and an intractable local recurrence.

A. Bucher (Vienna) said that seven patients with carcinoma of the bladder received local treatment with the drug and in three others it was injected intravenously. The growth of the tumor appeared to be checked for a while in some patients, and in others the tumor became smaller. While this treatment was being given, tenesmus rapidly subsided, and the patients felt better and gained weight.

F. Hesse reported that, for three years in Norderney, treatment with E-39 has been used in patients with cancer. The patients were given 5 mg. daily for several months and in one patient for over two years. In most patients the result was good. No damage to the myelopoietic system occurred, in spite of the prolonged treatment.

J. Kretz said that the toxicity of this drug as well as that of the disintegration products of the tumor should be kept in mind. Intravenous doses of 10 mg. of E-39 three times a week may quickly lead to an inhibition of growth. It is unwise to attempt to obtain a softening of the tumor in the shortest possible time. Impairment of the blood picture makes it imperative to stop intravenous injections, and direct injection into the tumor may lead to bleeding or perforation. A rapid disintegration of the tumor may also stimulate its growth. A longer treatment with smaller doses is, therefore, preferable. Sudden withdrawal of the drug may also be disastrous. Capsules for oral use may be given for a slow withdrawal of the drug. Tolerance for and efficiency of this treatment are increased by simultaneous general treatment with vitamins and dietary and medicinal protection of the liver.

P. Wurnig (Vienna) said that since drugs do not cure patients with extensive or advanced carcinoma, they were used as postoperative treatment of carcinomas radically operated on. An efficient but harmless drug that is easy to apply is required. Nitromin, a derivative of nitrogen mustard, was therefore used. The experiment was carried out in selected patients with carcinoma of the bronchi, since these patients have the most rapid downhill course. During the experimental period, all these patients underwent preventive treatment with Nitromin. The treatment consisted of three series of injections, each with a total dose of 700 to 800 mg. administered at intervals of from 6 to 8 weeks. The drug was well tolerated. The results showed that six months after the operation the life expectancy was 20% longer than in the untreated control group; one year later the life expectancy was 10% longer.

Radiotherapy of Tumors.—At the same meeting, A. Kohler (Munich) said that the value of preoperative irradiation of patients with cancer of the breast is now established. Of 459 patients who had preoperative irradiation of carcinoma of the breast in every stage, 41% were still living 10 years later. Delays of operation of one and one-half to five months are therefore allowed. Each daily dose devitalizes or inactivates cells of the carcinoma that are just dividing. Healing of the wound and recovery are normal, since a general but also a local recovery takes place between irradiation and operation. Favorable results with preoperative irradiation of patients with cancer of the breast were also obtained by W. Zaunbauer (Vienna), F. Melnizky (Salzburg), and E. Scherer (Marburg-on-Lahn) who pointed out that the skin condition is better with preoperative irradiation and that local recurrences and pulmonary fibrosis are less frequent. Although Melnizky does not use the usual interval between irradiation and subsequent amputation of the breast, his results are equally satisfactory and healing occurs without complications.

H. Stech said that the body is divided into six fields and every day one field is irradiated with 15 r. Undesirable general reactions and changes in the blood findings are thus reduced to a minimum. Duration and intervals of the irradiation depend on the blood findings and the prothrombin level. The patients are given up to four treatments with a total dose of 720 r at longer and longer intervals for one year. Teleroentgen-ray therapy combined with local inflammatory irradiation is particularly desirable for patients with generalized carcinosis, for patients in poor general condition with inoperable bronchial carcinoma, and, as prophylactic postoperative follow-up, in patients with a special risk of metastasis. In patients in whom recurrence cannot be prevented, prolonged disability associated with pains and increasing cachexia may be avoided by using this treatment in small doses. Death occurs rapidly after there has been a period of relative well-being.

K. Fochem (Vienna) said that carcinomas, stages 1 and 2, of the cervix uteri, as well as the operable carcinoma of the corpus uteri, were operated on and intensively irradiated using two abdominal and two gluteal fields. Inoperable carcinomas, stages 3 and 4, of the uterus were treated with 15,000 r of radium in three treatments. Following radical excision of ovarian and tubal carcinomas, patients are given postoperative x-ray therapy and local applications of radioactive gold. A patient with ovarian carcinoma whose operation was palliative is given one irradiation with 2,400 r. In patients with vulvar carcinoma, operation and irradiation are combined. It is possible to give up to 20,000 r with the filtration method. Massive doses of irradiation are essential, since a recurrent carcinoma after small doses of x-ray is resistant to therapy.

Serum Iron, Copper, and Transferrin Levels in Malignant Diseases.—At the same meeting, E. Gisinger said that in most patients with malignant diseases a decrease of the serum iron and transferrin level and an increase of the serum copper level occur simultaneously. This is particularly true in patients with Hodgkin's disease. If bleeding and, therefore, iron deficiency occurs, an increase of the transferrin level occurs, in spite of the presence of a malignancy, as an unequivocal diagnostic symtom of the iron deficiency. The individual leukosis can be distinguished to a certain degree since in patients with chronic leukemia the iron level in the serum is decreased, in those with the lymphocytic form the serum copper level is increased, and in those with granulocytic leukemia the levels are normal. Acute granulocytic leukemia is characterized by increased levels of copper and iron. Decrease of the transferrin level is found in patients with every form of leukemia. Patients with beta-myeloma have a normal serum copper level, whereas those with gamma-myelomas have an increased serum copper level. In 18 of a series of 23 patients with Hodgkin's disease, good results were obtained by cytostatic treatment. The size of the tumor decreased, the manifestations of Hodgkin's disease subsided, subjective complaints disappeared, and in some there was a complete regression of the inflammatory glands. The serum iron, copper, and transferrin levels returned to normal in three of these patients after treatment. The patients remained without recurrence four or more months. In five other patients, who showed no clinical improvement, the serum iron, copper, and transferrin levels did not return to normal.

Melanoma.—At the same meeting, G. Eichelter (Vienna) said that even a test excision in patients with pigmented nevi and melanoma may lead,

under certain circumstances, to metastasis, if malignancy is already present. No pigmented mole should be operated on without prophylactic irradiation. As far as is known r-ray contact irradiation does not produce metastasis. Up to 30,000 r may be applied if necessary. This therapy also gives excellent cosmetic results. Eventually additional irradiation of the regional lymph nodes may be given. If the skin disease is unchanged after the irradiation, excision may be performed more or less extensively under the protection of the previous irradiation with essentially less risk. Further treatment depends on the histological examination.

FINLAND

Deafness.—Siirala and Lahikainen (*Nordisk medicin*, July 4, 1957) examined the employees of a ship-building company, 185 of whom were exposed to loud noise while at work. They were classified in four groups according to the length of their employment. The first group included the workers whose exposure to industrial noise had lasted 10 years or less and the fourth group those whose exposure had lasted more than 30 years. It was found that the detrimental effect of noise continues as long as exposure to it lasts, and the worker does not get accustomed or inured to noise with the passage of time. After a person has been one year in a noisy occupation, his hearing has deteriorated as much as in three normal years. In other words, taking into account that these two types of deterioration of hearing are much alike, it may be claimed that the aging effect on hearing is three times as rapid in noisy as in quiet occupations.

Herpes Zoster Ophthalmicus.—The eye department of the Mellersta Hospital, Jyväskylä, serves a population of about 250,000 inhabitants and in the last three years has had occasion to deal with five cases of herpes zoster ophthalmicus. In *Nordisk medicin* for June 13, Dr. A. Oksala points out that the variety of remedies for this disease reflects the want of any specific remedy for it. He has not obtained satisfactory results with salicylates, posterior pituitary injection (Pituitrin), or ergotamine tartrate, and he has found that the value of antibiotics depends only on the elimination of secondary infections. Cortisone and hydrocortisone have been used only locally, and the effects have been satisfactory. The combination of cortisone with mydriatics is an improvement on earlier methods. Good results have also been obtained with injections of a liver extract with the cessation of pain and fever occurring in 24 hours. Should a second injection fail to achieve this effect, the treatment should be discontinued. Such injections apparently promote healing of the skin eruption and prevent postherpetic neuralgia.

Postural Hypotensive Collapse Caused by Chlorpromazine.—Stenbäck and co-workers (*Nordisk medicin*, May 16, 1957) studied the effects of chlorpromazine on 28 patients with special reference to the development of postural hypotensive collapse. They were subjected to Schellong's test which provides for measurements of blood pressure when the patient is in bed, standing up, and lying down. It was found that orthostatic hypotensive reactions to chlorpromazine given by injection four times daily take place mainly within the first 48 hours, but such reactions may occur even after 10 to 13 days. It was hoped that these examinations would give a clue to the likelihood of postural hypotensive collapse in a given case before chlorpromazine treatment was instituted. The need for such a prognostic clue is great because such collapse may prove fatal.

PERU

Institute of Biochemistry.—On March 23 the Institute of Biochemistry of the Faculty of Medicine of Lima was dedicated. Albert Baird Hastings, professor of biochemistry of the Harvard University Medical School, and representatives of the Kellogg and the Rockefeller foundations, two institutions that have contributed technical and financial assistance, attended the ceremony. Prof. Alberto Guzmán Barron has been named director of this institute.

Council on Mental Health.—In March the Ministry of Public Health created the Council of Mental Health, with Sebastián Lorente as president. Juvenile delinquency, a growing problem in Peru, will be studied intensively. Other pressing problems are the provision of more mental hospitals and the increasing of the availability of outpatient psychiatric services.

Mobile Medical Units.—Three mobile medical units have been purchased by the National Fund of Health and Social Welfare for about $40,000 each. They will be principally used for mass x-ray examination of the lungs, but they can also give minor medical, surgical, and dental care. Most of their work is being carried out in the poor suburbs of Lima.

Infectious Mononucleosis.—Dr. Castro Hoyos reported on 15 patients with infectious mononucleosis, 11 of whom were treated with prednisone or prednisolone (*Revista médica del Hospital Obrero*, vol. 5, no. 3-4, Dec., 1956). The age of the patients ranged from 2 to 14 years. The most prominent manifestations were fever, cervical or generalized adenopathy, sore throat, bronchitis, and rash, in that order. In the 11 patients treated with hormones, dramatic and prompt relief of symptoms was noted, the fever disappeared within 6 to 8 hours of starting the therapy, the general malaise and sore throat subsided completely, the hypertrophied lymph nodes became smaller, and pain and tenderness diminished or disappeared. The author called attention, however, to the absence of significant hematological changes after hormonal therapy. Furthermore,

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when given early, both hormones failed to prevent the appearance of the adenopathy and the rash. Cough was not affected by the hormones. The theoretical ground for the use of these steroids in the treatment of infectious mononucleosis is the well-known lympholytic effect accounted for by their glycocorticoid activity. The initial dose was 10 mg. four times daily. This was reduced slowly until a daily maintenance dose of 5 mg. was reached by the 14th or 15th day.

Medical Women's Association.—The first Latin-American medical women's association has been organized in Peru. The installation ceremony took place on July 8 at the Faculty of Medicine of Lima and was attended by the president of the nation, Manuel Prado, the minister of public health, and many prominent physicians. The membership of the organization is about 200, and its president is Dr. Suzy Roedenbeck, auxiliary professor of neuropathology at the Faculty of Medicine, San Marcos University. The purpose of the association will be to encourage and protect the medical interests of the Peruvian woman.

Chlorpromazine and Chronic Psychoses.—Dr. Querol and co-workers (*Revista de neuro-psiquiatria*, vol. 19, no. 4, Dec., 1956) reported on the treatment of 26 patients with chronic schizophrenia and 6 with chronic manic-depressive psychosis with chlorpromazine. Most previous reports on the value of this drug in mental conditions have shown the following: 1. It has a tranquilizing and sedative action on the patient's psychomotor agitation regardless of the origin of the agitation. 2. In the confusional states it reduces both the confusion and the delirium, and patients become well oriented and attentive. 3. It causes hallucinations to disappear. 4. In depressed states it causes the anxiety, feelings of indignation, and suicidal impulses to disappear. 5. In many patients with schizophrenia unresponsive to conventional treatment it causes either improvement or a social or complete remission of the disease. 6. Withdrawal of the drug is frequently followed by relapse, but good response is again obtained shortly after the therapy is resumed. The patients in the authors' series underwent chlorpromazine treatment alone or in combination with electroshock therapy and sedative medication. All patients received from 100 to 600 mg. of chlorpromazine daily long enough to modify their symptoms or for at least three months. Twenty-two of the schizophrenic and all of the manic-depressive patients had suffered from the disease more than one year. The remaining four schizophrenic patients had been ill from 6 to 12 months. In all the patients other previous treatment had failed. In the schizophrenic group, six patients were improved and four gained social remission and seven complete remission. Of the rest, eight were unchanged and one died. Four complete remissions and two deaths were observed in the manic-depressive group. None of the patients who died showed any benefit from the treatment, but no death could be directly attributed to the drug.

Catatonic and paranoid schizophrenia responded better to the treatment than did the simple and the hebephrenic types, and, in general, the results tended to be better in patients whose disease was of short duration. Recurrences of the symptoms occurred in three patients, but resumption of the treatment brought about prompt improvement. The authors believe that in refractory cases it is advisable to give the drug for as long as six months. Parkinsonism was the most frequent untoward side-effect observed in the patients treated with chlorpromazine. It was noted in 13 of the schizophrenic group and disappeared when the dose was diminished. In only a few patients was it necessary to discontinue the treatment temporarily. Obstinate constipation was another frequent secondary effect. Neither hepatic nor dermal complications were noted. Bronze pigmentation of the face was observed in seven patients. This side-effect, not reported before, cleared up slowly after the treatment was finished. The authors concluded that chlorpromazine must be regarded as the drug of choice for patients with endogenous psychoses, even though chronic. On the other hand, they pointed out that the psychological modifications produced by chlorpromazine do not equal those elicited by leukotomy.

Sanatorium for Tuberculous Children.—Peru's one and only tuberculosis sanatorium for children under 14 years of age was opened in 1950. Because its capacity was small (100 beds), most tuberculous children still had to be treated in a general hospital, with the consequent overcrowding of the children's wards in the latter. In March a 200-bed addition to the sanatorium was started. The new building will also include additional x-ray and laboratory equipment and a new electric-power plant.

UNITED KINGDOM

Annual Cancer Review.—The two main features of the annual report of the British Empire Cancer Campaign for 1956 are the increasing amount of work being carried out on the association between smoking and lung cancer and the rapid extension of the clinical uses of isotopes. Professor R. D. Passey and co-workers have failed, in spite of persisting efforts, to demonstrate any carcinogenic properties in the tar from cigarettes when applied to the skin of mice. A group of rats has been injected subcutaneously with English cigarette tar, and several series of hamsters have had a similar tar instilled into the trachea. In no instance in either species has any tumor arisen as a result. In further experiments in which groups of hamsters were exposed to the smoke of cigarettes for long periods daily in smoking machines some of the animals survived for 20 months without any evi-

dence of lung or other cancer. Although tracheitis, bronchitis, and bronchiectasis have been observed in rats subjected to the same condition, no tumors have arisen.

In other experiments, three groups of rats have been exposed, over a period of 10 months, to atmospheres containing cigarette and coal smoke and to a combination of the two. In none of these animals has any sign of neoplastic change occurred. The lyophilic, lyophobe, and phenolic fractions of tobacco tars have been painted on the interscapular region of 250 mice, and a crude tobacco tar has also been injected subcutaneously in 50 mice. Although the tests have been in progress for 21 months, no tumors have developed in either the painted or injected series. Professor Passey says: "During the last three years all those in Great Britain working on the effects of exposure to cigarette smoke or its tars have been consistent in reporting complete failure to demonstrate any carcinogenic action in a variety of laboratory animals, in spite of the proved presence of traces of the carcinogenic hydrocarbons in cigarette tars. This is in marked contrast to the reports from Wynder and his co-workers in America (1953, 1955). The difference in these results must be in the tars."

E. Boyland and D. C. Williams have continued their investigations of urinary beta-glucuronidase. Patients with cancer of the stomach, esophagus, rectum, breast, testis, and prostate have a higher than normal urinary beta-glucuronidase level, but those with cancer of the colon, thyroid, and kidney excrete normal amounts. A greatly increased urinary beta-glucuronidase activity is exhibited by patients with leukemia, Hodgkin's disease, cancer of the bronchus and prostate, and various types of cancer of the bladder (including those who have had their tumors removed and at the time of investigation have no active tumor). Prolonged treatment of patients with cancer of the prostate with diethylstilbestrol causes a great increase in beta-glucuronidase excretion. Since some nonmalignant diseases such as gastric ulcer, bronchitis, and coronary thrombosis also cause increase in beta-glucuronidase activity, the use of such activity as a diagnostic test for cancer is impracticable. Some evidence of therapeutic effect was obtained from the use of 2-chloro-ethyl methane sulfonate in 3 of 22 patients with terminal malignant disease. Forty-seven patients were treated with NN-di-(2-chloro-ethyl)-*p*-amino-L-phenyl alanine. In general, clinical results were disappointing, but there was recent evidence that intravenous administration may be much more effective. Three patients with chronic granulocytic leukemia have been treated with dimethyl busulfan. All have responded and are in remission.

The physics department of the Institute of Cancer Research reports the installation of the first British cesium unit, which was loaded in October with about 1,400 curies of cesium sulfate encapsulated in platinum. Preliminary studies were also made for a small cesium-137 unit suitable for treating lesions of the head and neck. It is apparent that, for this purpose, cesium-137 has several advantages over x-rays, radium, or cobalt-60. Yttrium-90 was used for radiation hypophysectomy, particularly in patients with mammary carcinoma. Two or three rods, 1.3 mm. in diameter and 4 mm. long, made of sintered yttrium oxide, each of activity of about 3 mc., are introduced into the pituitary under image amplifier control. Improved eye applicators of strontium-90 and yttrium-90 have been developed. These are satisfactory in clinical use, are durable, and have no constituents which may break down under irradiation. Work has continued on the applications in clinical radiography of low energy gamma-emitting isotopes, particularly radioactive xenon-133. Using high activity xenon sources, good radiographs of fractures of the wrist and ankle have been obtained with exposures of a few seconds. A technique of scintillation counting of alpha particles was developed for the measurement of low alpha activities in solid, liquid, or gaseous samples. This technique is proving remarkably simple, flexible, and consistent and is being used to estimate alpha activity in bones of persons who have lived in various environments and who have been exposed to special types of occupational hazard and in a variety of foodstuffs, soils, artificial fertilizers, and pharmaceutical substances.

New apparatus was designed and built for the intravesical administration of radioactive colloidal gold for the treatment of patients with multiple superficial papillary tumors of the bladder. A surface dose to the mucosa of 7,000 to 8,000 r (90% irradiation) is delivered over a period of 6 to 12 weeks in three separate treatment sessions lasting about three weeks each. In only a small proportion of patients so treated is the bladder rendered completely tumor free; in the remainder the tumor regression is usually of such an order that the small residual lesions can readily be treated by periurethral diathermy. Eighty patients with polycythemia were treated with phosphorus-32, the dose per injection ranging from 3 to 12 mc. The largest amount given to one patient was 47 mc. Ten of these patients died—five from intercurrent disease and five with leukemia or polycythemia present. In a program of research into calcium metabolism in malignant and nonmalignant bone disease, three patients have been studied so far. In one, radiostrontium was injected with the radiocalcium, and it was found that the 48-hour urinary excretion of strontium was five times as great as that of calcium.

At the Middlesex Hospital, 70 patients with cutaneous carcinoma induced by ionizing irradiations were studied. There were almost equal numbers of squamous and basal carcinomas which had arisen in patients previously treated by radiotherapy or exposed occupationally to ionizing irradiations. The most common disease so treated was lupus vulgaris, in which squamous cell tumors were found more often than rodent ulcers when malignant disease ensued. There were only 4 patients in whom squamous cell carcinoma developed in lesions of lupus vulgaris as compared to 16 in whom radiotherapy had been used in treating the lupus. Rodent ulcers were seldom seen after irradiation of lupus vulgaris lesions but appeared after depilation for ringworm of the scalp, sycosis barbae, or hypertrichosis of the face. In addition, four patients who were successfully treated by surgery and radiotherapy for mammary cancer developed rodent ulcers in areas of roentgen-ray dermatitis over the chest.

At St. Bartholomew's Hospital, intrapulmonary inoculations of known carcinogens and tobacco tar were made into the lungs of white rats, the material being injected directly around the root of the lung after the thorax had been opened. After methylcholanthrene had been injected, sarcoma occurred in 12 of 15 rats and after benzpyrene had been injected, sarcoma developed in 10 of 17, and in one an epidermoid carcinoma developed. In the series injected with methylcholanthrene, the average time between the inoculation and the death of the animals was 257 days, and in the series injected with benzpyrene, the time interval was 254 days. The same technique was used in investigating tobacco tar from a smoking machine and from a proprietary cartridge type of filter on sale in this country and believed to contain granules of silica-gel. About 10 cigarettes per filter were smoked by human subjects, the filters thereafter being washed out with acetone. Smoking-machine tar produced no tumors in a series of 10 rats, though the average time the rats lived was 464 days. Tar from the filters was injected into the lungs of eight rats; it produced one spindle-cell sarcoma in a rat that lived 607 days and one oat-cell cancer in a rat that lived 506 days.

Analyses of 39 brands of cigarettes from Austria, Bulgaria, Canada, Denmark, England, Finland, France, Germany, Greece, Italy, Norway, Poland, Rhodesia, Spain, Switzerland, United States, and Yugoslavia show that, as one passes eastwards in Europe, there is a fairly uniform decrease in the arsenic content of a cigarette weighing about 1 Gm. from as much as 100 mcg. to 1 mcg. or none. This is almost certainly due to the admixture of decreasing amounts of tobacco from the United States with increasing amounts of locally grown tobacco classed as "Turkish." Analysis of one of the most popular brands smoked in this country shows a fall in arsenic content from between 25 and 100 mcg. per cigarette in 1948-1949 to between 1 and 2 mcg. at present. This change appears to be due to the gradual abandonment of arsenical insecticidal sprays by tobacco growers in the United States.

At the Westminster Hospital, high-dosage pituitary seeding with gold radon seeds has been given up because of the poor results (average postoperative survival 3 months) and the number and severity of complications attending the procedure. As an adjunct to surgical hypophysectomy, however, radon seeds are left in the pituitary fossa. Sodium liothyronine combined with neomycin has been used, with encouraging results, as a local application in five patients with radiation necrosis. A new method of investigating the colloidal properties of urine has been evolved to study the protective action of such colloids. Preliminary results indicate that high concentrations of albumin or of mucoprotein are always associated with a high protective activity. This has been noted particularly in urines from patients with various malignant conditions, some of which have high mucoprotein levels. At lower mucoprotein levels, however, no correlation was present, and some pathological urines with normal protein and mucoprotein levels had a protective activity much above normal. The Marie Curie Hospital reported a 10-year follow-up of cancer of the cervix and of the body of the uterus treated by radium or a combination of radium and x-rays. Of 1,829 patients with cancer of the cervix, the 10-year survival rate was 30.2% of the patients treated, ranging from 69.7% for those in stage 1 to 4.4% for those in stage 4. The corresponding figures for the 308 patients with cancer of the body of the uterus were 36.4%, ranging from 86.4% to 13.4%. The records of this hospital showed that carcinoma of the vagina is a disease of later life, the greatest incidence being in the seventh and eighth decades. Thus, of the 79 patients treated in the hospital, 32 were in the seventh decade and 25 in the eighth decade.

St. Mark's Hospital reported that in a series of 4,500 patients with cancer of the rectum and colon, the operability rate was 75.6%, but in the first five years (1928-1932) it was 47.7% and reached 93% in the years 1953-1955. This steady increase in the proportion of patients operated on was attributed to the growing conviction that surgery not only prolongs life but also improves it. In a series of 120 colectomies undertaken for the treatment of ulcerative colitis, unsuspected cancer was found in seven cases, an incidence of 5.8%. A study of the relationship of carcinoma of the rectum and pregnancy indicated that pregnancy does not adversely affect the course of carcinoma of the rectum and that there is no indication for therapeutic abortion except when infection is anticipated and in some inoperable cases. Patients with carcinoma of the rectum diagnosed during pregnancy should be

treated in the same way as those who are not pregnant, except that, when the diagnosis is made in the last two months of pregnancy, operative treatment must be delayed until after delivery, which may be performed before term by cesarean section.

At the Hospital for Sick Children, 28 patients with histologically verified neuroblastoma were treated with vitamin B_{12}, the dosage in most cases consisting of 1 mg. given intramuscularly on alternate days for a period of two years when possible. Most of these children were selected for this treatment because no other mode of therapy offered any prospect of arresting the disease. Of these 28 children, 13 died without showing any significant response. The rest all showed definite evidence of tumor arrest or regression. In nine patients this was maintained for periods of from seven months to six years from the inception of treatment and all nine were alive when last seen. The observation of regressive phenomena in 50% of the patients treated in this series is greatly in excess of that occurring spontaneously (probably 1 to 3%). Regression was observed only in those with a clinical onset in infancy. There were only two instances of remission in the older age-group, despite the fact that the latter represented 50% of the total series.

P. M. F. Bishop is investigating the alleged carcinogenic effect of prolonged administration of estrogens by following up a series of 840 patients who, between 1937 and 1953, had a minimum of six months' treatment with estrogen. Of the 420 patients so far traced, only one had adenocarcinoma of the uterine body, and one had carcinoma of the breast. Ten women have died, and in none of these was there either a mammary or genital carcinoma. A further 220 patients with a definite history of metropathy or menorrhagia, i. e., patients with an excessive amount of endogenous estrogen, are being studied. Of the 120 so far traced, 38 (30%) have undergone hysterectomy; 8 showed definite evidence of cystic glandular hyperplasia; and 8 showed some evidence of hyperplasia. None had any evidence of malignancy. Another approach to the problem was through a study of 88 unselected patients with carcinoma of the uterine body. Only three of these had received estrogen therapy for more than a year preceding the diagnosis of malignancy.

Preliminary results of investigations into the smoking habits of women with lung cancer living in urban and rural areas of North Wales, Cheshire, and Lancashire, according to Percy Stocks, support the previous findings for men that both smoking and urbanization are independently related to lung cancer mortality.

A report on the conference on estrogen methodology, organized by the British Empire Cancer Campaign, stresses that any satisfactory quantitative estrogen methods must be very complex and technically difficult and that therefore they should not be lightly undertaken with inadequate facilities. The two currently used methods critically examined at the conference are unsuitable for routine use in a hospital laboratory. They were designed for use in specially equipped and staffed laboratories, as the precision and accuracy of which they are capable can only be attained under these conditions. The publication of results obtained by any method for the determination of urinary estrogens by workers who have not themselves determined the precision and accuracy of that method is to be deplored.

Family Physicians Feel Let Down by Some Consultants.—Sir Russell Brain, past-president of the Royal College of Physicians and one of the joint chairmen of the doctors' negotiating committee, in the recent claim for a 24% pay increase, was criticized at the British Medical Association's annual meeting at Newcastle-upon-Tyne. A split in the profession was feared. Many family physicians believed that, in their dispute with the government, they had been let down by some of the specialists of Harley street. The charge against Sir Russell was that he had indicated that, in the event of pay talks with the government breaking down, the decision as to the action to be taken would not be made by the B. M. A. alone. In conversation afterwards, many physicians deplored the attack on Sir Russell. The B. M. A. maintains that the Spens reports place a moral obligation on the government to increase doctors' pay as the cost of living rises. The government rejects this interpretation. A motion by Dr. H. G. Dowler asked that, as moral obligations had evidently ceased to be obligatory, in future only terms of service in the National Health Service enforceable in law should be accepted. Dr. Solomon Wand, chairman of the B. M. A. council and a principal negotiator in the dispute with the government over pay, said that the government had indicated that the physicians' claim could not be considered on its merits because it would have such inflationary results. This might have seemed a fair assumption had not the members of Parliament a few days later voted themselves a substantial raise. Dr. C. P. Wallace proposed the resolution which led to the attacks on Sir Russell Brain. He moved that it was improper for any individual member of a joint negotiating committee to take independent action without the prior consent of the whole committee. There were cries of "Why?" when Dr. Wand described Dr. Wallace's speech as unfortunate. "Because," he replied, "we are not recriminating on the past; we are looking to the future." A motion to pass to the next business was defeated. Dr. G. Cormack said, "If Dr. Wallace's speech was construed as an attack, that was all to the good. I hope you will pass this as a vote of censure on the man concerned and as a warning to other people who might be of the same mind in the future." The motion was carried.

CORRESPONDENCE

HEALTH IN THE HEAVENS

To the Editor:—Physicians and their scientific colleagues in aviation medicine will be gratified by the intelligent and stimulating review of the current status of space travel, "Health in the Heavens" (*J. A. M. A.* **164:**765-769 [June 15] 1957), and by the accompanying editorial in the same issue. To paraphrase the statement of Dr. John F. Fulton in the foreword of "Doctors in the Sky" (Charles C Thomas, Publisher, 1955), the future of the specialty of aviation medicine today appears as boundless as the skies its practitioners are exploring.

A minor error was noted in this excellent article. Dr. John Jeffries accompanied Jean Pierre Blanchard in the first balloon flight across the English Channel on Jan. 7, 1785, not 1795. Earlier, on Nov. 30, 1784, he made an ascension over London. Also, Dr. John P. Stapp recently was given a well-deserved promotion to colonel in the Air Force Medical Corps.

Few physicians will read "Health in the Heavens" without a feeling of pride in the part their profession is contributing to space travel. Likewise, few will doubt that space flight will soon be here—and probably to stay.

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MOUNTAIN CLIMBING

To the Editor:—The Leisure Corner article on mountain climbing in the Aug. 3 issue of THE JOURNAL, page 1609, was interesting. If it was intended as an introduction, it is probably adequate for eastern mountains but not for western. For fear real mountaineers are out climbing or are too modest to offer suggestions, may an amateur warn beginners about two items of equipment? Climbing in the Rockies above the timberline consists in rock work, and leather-soled shoes are too slippery. Rubber, composition, or similar materials cling to rock and are much safer. Probably most who go onto snow and ice use crampons (removable iron spikes) rather than cleated or nailed soles. Rope work should not be undertaken by beginners without adequate demonstration and instruction. Many prefer the new nylon rope, as it is lighter, stronger, more elastic, and more pliable when wet than hemp. The best way to start is to join a mountain club for a prolonged outing for a week end or longer. The Alpine Club in New York City will gladly furnish information on the closest club or on one in the vicinity of the proposed climbing area.

Colorado mountaineers are probably chagrined to have Montana and Wyoming credited with scores of peaks between 10,000 and 13,000 ft. and Colorado with only Pike's Peak, which has a car road to the top, when, according to the Encyclopædia Britannica, Colorado has "52 of the 67 highest mountains in U. S., all over 14,000 feet." They would prefer mention of their highest peak, Mount Elbert (14,431 ft.) or the peak probably most climbed on foot, Long's Peak (14,225 ft.) and its noted and notorious East Face, 1,625 vertical feet, which is beyond amateur mountain hiking.

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PAIN AND PLACEBOS

To the Editor:—In a paper entitled "Codeine Phosphate, Propoxyphene Hydrochloride, and Placebo" published in the June 29, 1957, issue of THE JOURNAL, page 966, Gruber refers to some work published by my colleagues and me in 1954 (*Am. J. Med.* **16:**770 [June]). Gruber implies that we observed some sort of diminishing efficacy with morphine and with placebo over a period of time. He states that we saw "increasing pain" when placebos were given. I have observed no diminution in the effect of the placebo doses with the passage of time in any studies in which I have participated; on the contrary, placebo and morphine each seem to perform better toward the end of the period of postoperative pain than in the beginning of this period. What we did observe was a definite correlation between duration of pain, severity of pain, and efficacy of morphine or placebo.

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Baltimore 5.

HABIT-FORMING DRUGS

To the Editor:—In Foreign Letters in the July 13 issue of THE JOURNAL, page 1268, is a short note from France reporting on the effects of a new analgesic 2,2-diphenyl-3-methyl-4-morpholine-butyryl-pyrrolidine (R 875), prepared by P. Janssen of Belgium. The note says, "It is not habit-forming." This product has been studied in the United States, including tests at the Addiction Research Center at Lexington, Ky., with the conclusion that it "has addiction liability at least equivalent to that of morphine (Addendum to the Minutes of the 18th Meeting of the Committee on Drug Addiction and Narcotics of the National Research Council). R 875 was placed provisionally under international narcotics control by the Commission on Narcotic Drugs of the United Nations at its 12th session, and coverage of R 875 under the U. S. Opiates Act has been recommended.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Governmental Hospitals: Liability for Negligence of Employees.—This was an action for damages against a county hospital and its trustees and superintendent for injuries to a pay patient allegedly caused by the negligence of a hospital employee. From a judgment in favor of the hospital the plaintiff appealed to the Supreme Court of Iowa.

Is a county hospital liable for injuries to a patient caused by the negligence of a hospital employee? Under the ancient common law, said the court, the sovereign, generally speaking, could not be sued and this policy is now found in the Iowa statutes. The state is thus immune from suit. Counties, however, are creatures of legislative enactment and may sue and be sued. They are not, as a rule, held liable for torts committed by them, so long as they are acting within the scope of their governmental powers. The difference between a governmental and a proprietary function is that in its governmental function the county is made, by the state, one of its instruments, or the local depository of certain limited or prescribed political powers, to be exercised for the public good on behalf of the state, rather than for itself; while in its proprietary function the theory is that the powers are supposed not to be conferred, chiefly or primarily, from considerations connected with the government of the state at large, but for the private advantage of compact community, which is incorporated as a distinct legal personality or corporate individual.

The defendant hospital was established under Chapter 347 of the Iowa Code. Neither that chapter nor any other statutory provision, said the supreme court, requires a county to provide facilities to care for the sick or infirm, whether indigent or not indigent. Whether or not there shall be a county hospital rests entirely with the county's residents and any assumption of such power is purely voluntary. Under Chapter 347, continued the court, the powers thus assumed are clearly intended, at least primarily, for the private advantage and benefit of the locality and its inhabitants. The majority view is that the operation of a hospital under such circumstances is a governmental function which grants immunity but the tendency is to deny immunity where injury results from negligence of officials or agents exercising purely ministerial powers. The operation of a hospital by a county under Chapter 347 is a proprietary function, at least so far as a pay patient is concerned, said the court, and should be considered in the same light as a private hospital, which, according to well settled law in this state, is liable in tort for injuries to pay patients injured through the negligence of their employees. The motion to dismiss rested on the contention that defendants were merely agents of the county and performing a governmental function, and were, therefore, entitled to the same immunity as the county. Since the court concluded that the county has no immunity, its agents, necessarily, have no immunity either. The judgment of the lower court in favor of the hospital was accordingly reversed and the cause remanded. *Wittmer v. Letts, 80 N. W. (2d) 561 (Iowa, 1957).*

Malpractice: Need for Consent Prior to Plastic Surgery—Minors.—The plaintiff filed a suit for damages for malpractice and assault and battery against the defendant physician for performing a plastic operation on her nose without her consent. From an adverse judgment the plaintiff appealed to the Supreme Court of Ohio.

This appeal concerned only the assault and battery count, the malpractice count having been dismissed by the trial court. The primary issue was whether or not a minor can sue in an assault and battery charge for an operation to which her parents or guardian did not consent.

The plaintiff, 18 years old but a minor under Ohio law, sought out the defendant physician in response to an ad in the telephone directory, "Reshape Your Nose in Plastic Surgery." After an interview and examination the defendant physician operated upon the plaintiff's nose. The defendant physician testified that at the time of the operation the plaintiff told him that she was 21 years old and that she called at his office on several occasions for follow-up treatments. Subsequently, however, she filed suit against the defendant claiming that, as a result of the assault and violation of her bodily integrity, permanent changes in the tissues and structure of her nose were made with a detrimental effect upon her physical appearance, and that she was caused to suffer mental shock, humiliation, depression, and a general personality and nervous breakdown so that she could not return to her employment.

The term "consent," said the Supreme Court of Ohio, as used herein carries with it the assumption that previous full disclosure of the implications and probable consequences of the proposed conduct to which such consent applies has been given in such terms as may be fully comprehended by the person giving the consent. Continuing, the court said that the general rule seems to be that, unless there exists an emergency, which prevents any delay, or other exceptional circumstances, a surgeon who performs an operation upon a minor without the consent of his parents or guardian is guilty of a trespass and battery. This rule is not based upon the capacity of a minor to consent, so far as he is personally concerned, within the field of the law of torts or law of crimes, but is based upon the right of parents whose liability for support and maintenance of their child may be greatly increased by an unfavorable result from the operational procedures upon the part of a surgeon. The court further pointed out, however, that in the present case the plaintiff was only entitled to recover nominal damages. It therefore reversed the judgment in favor of the

plaintiff because more than nominal damages had been awarded by the trial jury. *Lacey v. Laird, 139 N. E. (2) 25 (Ohio, 1956).*

Insanity: Privileged Character of Physician's Testimony.—This was an action against the defendant physician for damages suffered as a result of a detention, following emergency detention proceedings, in a state hospital on the basis of the defendant's allegedly erroneous certificate. From a judgment in the trial court overruling his demurrer, the defendant appealed to the Supreme Judicial Court of Maine.

According to the law in Maine, said the Supreme Judicial Court, municipal officers are authorized to issue immediate restraint and detention orders when such is necessary for the person's comfort or safety or the safety of others providing the complaint is accompanied by physicians' certificate. An examination and certificate of insanity by two reputable physicians is, under the law, a mandatory requirement. Continuing, the court said that, construing the statute as a whole, the certifying physician is a witness in emergency restraint and detention proceedings and the municipal officers are judges. A witness in a judicial proceeding, said the court, is absolutely privileged to publish false and defamatory matter about another as a part of a judicial proceeding in which he is testifying if the defamatory matter is relevant to the subject or inquiry. Therefore, the court concluded, the certificate of the defendant was privileged and his demurrer to the complaint should have been sustained. The judgment of the lower court was accordingly reversed. *Dunbar v. Greenlaw, 128 A. (2d) 218 (Maine, 1956).*

County Hospital: Liability of County for Negligence of Hospital Employee.—This was an action for damages against the county, the county commissioners, and an employee of a hospital established by the county allegedly due to the negligence of the employee. From a judgment for the defendants, the plaintiff appealed to the Supreme Court of Nevada.

The hospital in which the injury occurred was established by the county pursuant to the laws of Nevada and, in a prior suit, it was held that a hospital established pursuant to such laws is not a legal entity and is, therefore, not subject to suit. However, said the Supreme Court, it does not follow from the fact that the hospital is without independent legal entity that there is no public responsibility for torts committed by its employees. The hospital is an institution established, owned, and supported by the county. Having no entity apart from the county, it must follow that the county is the party legally responsible for obligations of the hospital. The county contended that this could not be true in this case because, by statute, the control of the hospital is vested in the trustees elected by the voters of the county and the county commissioners have no management powers. The court said that the fact that the county commissioners are without managerial control does not deprive the county of representation or control or relieve it of liability. The hospital trustees are officers of the county, representative of the county, and responsible to it within their limited sphere of authority to the same extent as are the county commissioners within their general sphere. A county may operate through such agencies as the legislature directs. Accordingly, the judgment in favor of the defendants was reversed and the cause remanded. *Hughey v. Washoe County, 306 P. (2d) 1115 (Nev., 1957).*

Dead Bodies: Who May Authorize Autopsy?—This was an application by the sisters of a decedent for an order authorizing an autopsy on his body for the purpose of determining the cause of death. The decedent's widow filed a motion to dismiss the application, which motion was granted, and the applicants therefore appealed to the Supreme Court of Oklahoma.

The Oklahoma statutes provide: "The right to dissect the dead body of a human being exists . . . whenever any husband or next of kin of a deceased person, being charged by law with the duty of burial, authorized such dissection for the purpose of ascertaining the cause of death." The statute relating to the duty of burying the body of a deceased person specifically provides for those instances in which a married woman dies by placing the duty of burial on the husband or, in the event of his prior death, on the nearest kin. If the deceased is not a married woman, the statute places the duty of burial on the nearest kin, with no mention of a surviving widow. The applicants, therefore, contended that their rights superseded those of the surviving widow since they are the nearest kin.

The Supreme Court said that, as between the wife and other relatives, the great weight of authority is that the care and custody of the body and the right to provide burial rests, in the first instance, with the surviving spouse. The applicants argued that, if the legislature had intended to include the wife, the word "spouse" instead of "husband" would have been used in the law. They argued that the language of the law must be strictly construed, thus depriving a surviving wife of any right or voice in the disposition of the remains of her deceased husband. This, said the Supreme Court, is tantamount to saying that it was intended by the act to make the duty of burial of a deceased person that of a stranger, to the exclusion of a surviving wife, since the law which makes no mention of any surviving spouse, except the "husband," goes so far as to provide that the duty of burial develops upon the tenant, or, if there be no tenant, upon the owner of the premises where death occurs or the body is found. The court held that it was unable to conceive that the legislature, by either reason or necessity, intended any such result. Continuing, it said that courts will not follow the letter of a statute where the literal meaning would lead to absurd consequences which the legislature could not have contemplated. They are bound to presume that such consequences were not intended and to adopt a construction which

will promote the ends of justice and avoid the absurdity. The terms "kindred" and "next of kin" as used in the law include a relationship existing by reason of marriage. The applicants, therefore, did not have the primary right of burial over the surviving widow. The judgment of the lower court dismissing the application of the decedent's sisters was accordingly affirmed. *In re Kyle's Autopsy, 309 P. (2d) 1070 (Okla., 1957).*

Charitable Hospitals: Termination of Staff Privileges.— The plaintiff, a physician, filed an action against the defendant, a nonstock hospital corporation, for a declaration that his dismissal from the hospital staff was of no effect, and asking that the trustees be enjoined from depriving him of his rights as a member of the medical staff. From a judgment for the hospital, the plaintiff physician appealed to the court of appeals of Maryland.

By way of background, the evidence showed that the plaintiff and his brother, in addition to practicing medicine, carried on an active real estate business. In 1938, they purchased property which they used as their offices and a small hospital. In 1941, the plaintiff and some associates incorporated Doctors Hospital, Inc., as a nonstock corporation. From 1938 to 1947, the plaintiff's family financed the hospital and made up its board of trustees and the hospital was managed by the plaintiff exclusively. In 1944, Doctors Hospital, Inc., bought property which it intended to convert into a hospital. Because outside capital could not be attracted to a nonprofit corporation, the plaintiff formed Doctors Hospital of Maryland, Inc., a stock corporation. The money from the sale to the plaintiff, his brother, and three other physicians of the stock of this corporation and the proceeds of a mortgage were used to build the present hospital. Operations were begun in the new building in 1947 with the plaintiff personally in control of all operations. When the hospital tried to gain membership in the Maryland Hospital Association, commonly known as Blue Cross, it was learned that this could not be done if the hospital was operated by those who controlled it financially. Doctors Hospital of Maryland, Inc., therefore transferred all its assets to Doctors Hospital, Inc., and was thereafter dissolved. The plaintiff testified that, as part of this transfer, Doctors Hospital, Inc., assumed all obligations of the stock corporation and that he and another physician were given permanent rights to be members of the hospital and its staff. In 1948, a mortgage was executed from Doctors Hospital, Inc., to the plaintiff and his wife on which there is now $100,000 owing. When the hospital sought accreditation from the Baltimore City Medical Society, acting as agent for the American Medical Association, it was told its board of trustees was too small and should be expanded to 15 members, with backgrounds of public service and with no previous business affiliations with the hospital or its staff. The plaintiff, his brother, and two others resigned from the board and new members were elected to take their places. The plaintiff was appointed administrator of the hospital and continued in that position until 1951, when he resigned pursuant to the recommendation of the Baltimore City Medical Society that he do so on the ground that he should not be the executive officer of the hospital while he was on its staff and while it was heavily obligated to him financially. From 1951 on there was friction between the plaintiff and the board of trustees which culminated in the board's refusal to renew the plaintiff's staff privileges.

The plaintiff contended, among other things, that his dismissal was invalid because it was without notice to him and he had no opportunity to be heard. This was based, said the court of appeals, on the contention that he was dismissed for cause, and that in such case the bylaws of the medical staff required notice and hearing. We think this misconceives what occurred, said the court. The plaintiff challenges the validity of the pertinent bylaws of the medical staff adopted by the board in November, 1954, but both before and after November, 1954, the bylaws of the medical staff provided that appointments should be for the calendar year in which the appointment is made. Plaintiff was not dismissed during the year. He was merely notified that his year to year privileges would not be renewed when they expired. In such case no notice, other than that given him, and no hearing, are required. In Levin v. Sinai Hospital of Baltimore City, 186 Md. 174, this court held that a private hospital has the right to exclude any physician from practicing in it and that such exclusion rests with the managing authorities, adding that the directors of a private hospital corporation who have the power to appoint members have the power to remove them from the staff. In that case the court concluded "It is clear, therefore, that since the bylaws of defendant provide that appointments to all divisions of the medical staff shall be made for only one year, appellant has no right to object to his removal from one of the divisions of the staff." We think, concluded the court of appeals, the procedure followed by the board in allowing plaintiff's privileges to expire at the end of the year without renewal was fully in accord with the bylaws of the medical staff and the principles of the Levin case.

The plaintiff also contended that the action of the board was arbitrary, capricious, unwarranted, and unjust. We agree with the chancellor that there was no basis for such a charge, said the court of appeals. The record is replete with evidence that the plaintiff was an obstacle to the control of the hospital by the board, that he was not amenable to discipline, which he often required, and that his presence led to an inharmonious working of the hospital. It is clear that he was either unable, or refused, to comport himself effectively and agreeably within the framework of a charitable hospital conducted on a high plane by a public spirited and sincere board of trustees, as such hospitals generally are conducted and that this attitude

created the situation which justified the exercise of an honest discretion by the board leading to his elimination from the scene.

The plaintiff's other contentions were of a more or less technical nature relating to the intent, purpose, and meaning of certain documents adopted by the board, certain documents which passed between the board and the plaintiff, and certain actions taken by the board pursuant thereto. These contentions were also resolved in favor of the hospital. The judgment of the trial court refusing the plaintiff's requests was therefore affirmed. *Glass v. Doctors Hospital, 131 A (2) 254 (Md., 1957).*

Malpractice: Postoperative Care Following Removal of Gall Bladder—Need for Expert Testimony.—This was an action for damages for injuries caused by the alleged malpractice of the defendant physician. The trial judge set aside a jury verdict in favor of the plaintiff and entered judgment for the defendant, so the plaintiff appealed to the Supreme Court of Utah.

The defendant removed the plaintiff's gallbladder; there was no negligence in the performance of the operation. Following the operation, however, the plaintiff suffered pulmonary complications allegedly culminating in a collapsed lung, causing pain and suffering and resulting in loss of employment, all of which she attributed to lack of postoperative care. The plaintiff contended generally that the defendant's postoperative care was negligent in that he failed to observe elevation of pulse and temperature and to take remedial measures, that he failed to observe the pain plaintiff suffered, which required sedation, and that he failed to take x-rays to determine the cause of continued chest pains. None of these claims of negligence, said the Supreme Court, was supported by any expert testimony. Whether an attending physician exercised the ordinary care, skill, and knowledge required of doctors in the community which he serves, continued the Supreme Court, must ordinarily be established by the testimony of physicians, except when the facts may be ascertained by the ordinary use of the senses of lay witnesses. Care of a patient after a gallbladder operation, however, depends upon complex scientific knowledge and cannot be ascertained by common lay knowledge.

The plaintiff's principal contention of negligence in postoperative treatment was that she was not "turned and coughed" in accordance with accepted medical standards. The defendant, testifying as an adverse witness, explained that after upper abdominal surgery, when the abdominal muscles are painfully used, the tendency exists to breathe shallowly and if this continues a partial filling of the lung cells and an eventual collapse of the lung may result. Deep breathing and coughing, he said, tend to loosen the accumulated matter and aid in using the full capacity of the lung. The defendant further testified that the medical standards of physicians within the community would require coughing and turning somewhere between every two hours, the routine maximum standard, and every six hours, the minimum standard. The hospital record does not specifically note that the plaintiff was "turned and coughed" as such as often as once every two hours, admitted the Supreme Court, but it does show orders entered and services rendered which necessarily involved movements of the abdomen and chest, such as giving shots, baths, and enemas; "being made comfortable"; inserting rectal tubes; and being catheterized. In fact, the hospital record disclosed 18 of such services in a period of 43 hours. In view of this evidence, continued the court, no finding could reasonably be made that the patient was not turned and coughed at intervals sufficiently frequent to meet even the maximum standard testified to by the defendant. Furthermore, the court pointed out, the defendant gave orders for regular turning and coughing as well as for other treatment and medication. If such orders were not carried out, the failure to do so was the responsibility of the hospital personnel and not the defendant, unless the knowledge of such laxity was in some manner brought to his attention and he failed to take steps to remedy the situation. There was no evidence that the defendant had such knowledge. The judgment of the trial court in favor of the defendant physician was accordingly affirmed. *Huggins v. Hicken, 310 P. (2d) 523 (Utah, 1957).*

Malpractice: Trial Court's Instruction as to Effect of Malpractice Judgment on Physician's Reputation:—This was an action for damages for injuries caused by the alleged malpractice of the defendant physicians. There was judgment for defendants and the plaintiff appealed to the Supreme Court of Florida.

The plaintiff contended that the trial court erred in giving the following charge to the jury at the request of the defendants: "In a case against a physician for malpractice, the professional character and reputation of the physician is the most important matter at stake, and hence he should not be condemned by evidence that does not point to his negligence." If the trial court had allowed physicians to testify that a judgment against a physician in a malpractice case would result in great injury to the professional character and reputation of a physician, the admission of such testimony would have required a reversal, said the Supreme Court. The giving of the questioned charge was an even greater error because it was a statement by the trial court to the jury that, in considering their verdict, even should they conclude that the physicians had been negligent and that such negligence proximately contributed to the plaintiff's injuries, they were entitled to weigh against that the effect that their findings and verdict would have upon the professional character and reputation of the defendants. The court held that the giving of such charge was reversible error because it misled the jury. Accordingly, the judgment of the lower court in favor of the defendant physicians was reversed and the cause remanded. *Stauf v. Holden, 94 So. (2d) 361 (Fla., 1957).*

MISCELLANY

The following article was prepared by the valedictorian of the 1957 graduating class of the Olivia, Minn., High School. She received $1,000 for winning first prize in the National Essay Contest which is sponsored by the Association of American Physicians and Surgeons in cooperation with state and county medical societies. The author intends to use her prize money as a premedical student at the University of Minnesota.—ED.

THE ADVANTAGES OF PRIVATE MEDICAL CARE

Sonia Gustavson

"May the love for my art actuate me at all times; may neither avarice, nor miserliness, nor thirst for glory, nor for a great reputation engage my mind; for the enemies of Truth and Philanthropy could easily deceive me and make me forgetful of my lofty aim of doing good to Thy children."[1]

The art of medicine is the Great Art. Its practicers are dedicated; its appreciators are fervent. Surely it is the wish of all thinking, discerning men that members of the medical profession know an atmosphere which will enable them to maintain the high quality of health care that they are giving Americans at the present time. That atmosphere is one which is free from government control or intrusion. American medical men possess this freedom now, and they must continue to possess it. . . .

Since the founding of our nation, life expectancy has increased 39 years. . . . Since 1900, the death rate has increased for 8 diseases, while it has decreased for 21. . . . The increase is due to the fact that, since that year, the population of America has doubled. For every 1,000 babies born in 1957, some 130 live who would have died 50 years ago. The number of people over 65 has quadrupled, and these people account for the marked rise in the death rates for cardiovascular diseases, cancer, and other diseases of old age. The decrease is due to the discovery and perfecting of antibiotics, improved surgical methods, quicker diagnosis and reporting, and to the work done in the field of preventive medicine.

Such splendid achievements could not arise from a profession with low standards of quality. The medical profession requires of its prospective members ten years of advanced education in any of the nation's 82 approved medical schools and under intern and residency programs. Post-graduate courses are offered by schools, societies, hospitals, and other health agencies. Standards are elevated in auxiliary fields of medicine such as laboratory technology and occupational therapy. Financial aid can be secured by deserving medical students. A record number—7,686—entered medical schools in the 1955-56 academic year. What may appear to be, in some areas, a shortage of doctors, in actuality is maldistribution. This is being remedied by placement programs which inform communites of doctors desiring locations and inform doctors of communities desiring medical care.

One of the arguments for socialization of medicine frequently used by uninformed people is this: "If the government takes control of medicine, we'll get free medical care." Medical care, like every other necessity, costs money. There is no reason why anyone should hesitate to go into debt to meet medical costs. There are three ways that a man can pay for medical care. (1) Cash. It is cheaper to pay for home or office calls than to pay taxes to the government on the chance that you might need this kind of service. (2) Savings, securities, loans. Should a man find it necessary to delve into his savings to pay a medical bill, he can do so. If this is not necessary, the savings will remain on hand to meet other types of expenses that may arise. If medical bills were met with federal taxes which are, in this case, compulsory savings, a man could not use these funds for any purpose other than to meet medical expenses. (3) Commercial insurance. In exchange for premiums, you are paid for the costs of more serious illnesses and operations. The uncertainty of a large expenditure is replaced by the certainty of a small one. The advantage of voluntary health insurance over compulsory health insurance is this: The individual reserves the right to select his own doctor and hospital. At the present time, over 60% of the estimated eligible population carries some type of voluntary hospital expense coverage, and approximately 50% is protected against some of the insurable costs of surgery. The voluntary health insurance movement has already surpassed the goals originally charted by the pioneers in the field. It has been on a voluntary basis that all great progress in America has been achieved, and only on that basis can the nation be assured of progress in this field.

A look at the country of England will show us some of the dire results of the socialization of medicine. Under the National Health Program, that country proposed to give the indigent, the poor, the average, and the wealthy the same quality and quantity of medical care, and maintain the quality and quantity that the wealthy were accustomed to under private practice. What happened? In London, wealthier districts have an average of one doctor for 1,261 patients, and poor districts have twice as many patients per doctor. The farming and mining communities suffer even more from lack of medical services. In February of this year, the British Medical Association advised 21,000 English general practitioners seeking a pay raise to quit Britain's socialized system of medicine. The Association recommended . . . a pay-as-you-go plan.

From bitter experience, Britain has learned some of the inevitable results of government medicine. (1) Administrative costs of collecting the taxes and re-distributing them as sicknesses occur make the entire program less than worthwhile. (2) The physician-

patient relationship, always confidential, has been disturbed by this third party intruder, the government. (3) Physicians lose autonomy in diagnosis and treatment that they possess in private practice. (4) Political influences enter into the sphere of medicine. (5) Regimentation occurs in conditions of employment for doctors: the number of hours they must work, their income, and their location. (6) Standardizing the treatment of patients slows down research.

Should anyone feel that the indigent and the chronically ill are being neglected under America's present system of medicine, let us investigate these areas. The chronically ill are, of course, excluded from private medical plans because the risk is too great. However, in this country there are private institutions that give considerable amounts of aid to the aged, the sick and the handicapped. Doctors often treat these people at reduced costs. Indigent people . . . are the only people who should receive government aid. If the government stepped in to furnish all of us with medical care, all private resources would dry up and the taxpayer would have to shoulder the entire load. The government already takes one-third of our income, so why make it necessary for it to take more, when private medicine is less expensive and so much more efficient. Let us not forget that it is the intrinsic nature of bureaucracies to get bigger and bigger, more and more wasteful, costlier and costlier and, at the same time, to get further and further out of touch with the individual and his or her particular needs.

In 1939, in a small country town, a woman was stricken with simultaneous influenza and pneumonia. For several days her life hung by a thread, and during these days her family doctor . . . was available to administer stimulants when it seemed the thread could hold no longer. As a last resort, this country doctor sent to a larger city for a new drug that had just appeared on the medical scene which, through his constant studying, he had just learned about. This forerunner of the "miracle" drugs—sulfanilamide—along with the doctor's dedicated care, saved the woman's life.

Picture the same case under socialized medicine. During the day, the doctor would have been too harassed by petty rules and regulations of diagnosis and treatment to give his undivided attention to the saving of this life. After hours, when stimulants were needed immediately, the "night doctor" would have had to have been called. In all likelihood, there would have been no case-continuity nor any of the vitally important feeling for the patient on the part of the "night doctor" working his "shift." When the new drug was wanted, there would have been red tape to cut, and forms and requisitions to fill out. By the time the drug would have arrived, the thread of life would have been completely and finally severed.

When I see this woman now . . . it seems to me that she is a living embodiment of the advantages of private medical care.

References

1. Maimonides: Daily Prayer of a Physician.

THE LEISURE CORNER

CREATING A LIBRARY OF MUSIC RECORDS

Interest in recorded music has shown such tremendous growth in recent years that home record libraries have become an invaluable and meaningful hobby. While trained musicians and seasoned concert-goers know precisely what music they want to own, there exists a large group of persons, including physicians, who have an innate love of music but who hesitate to venture beyond the realm of the semiclassical or popular song hits. By starting a record collection, these individuals can readily increase their understanding and love of the classics through repeated playing of music that has been recorded by outstanding interpreters.

To be "at home with music" by virtue of a library of records implies establishment of an unashamed expression of personal taste. This has not always been true of specially trained and privileged music lovers of the past. Listening to music was often regarded as a duty rather than a pleasure, an earmark of cultural and social superiority. Today, to the purchaser of music records, listening to these records takes on the added pleasure of independence of selection. This type of person is not necessarily concerned whether he is found in the company of other music lovers, nor does he have to go into a technical discussion of musical details. He merely purchases music that he likes or that has been recommended to him by those whose opinion he respects. The fact that he willingly pays for his recorded music is self-explanatory. It is only out of the care that he devotes to creating a musical library, without cluttering up a household with albums that represent false musical pretensions rather than personal selection and taste, that pleasure actually comes.

In creating a library of music records, it is best to commence with music that you know and like. Then, going on from this vantage point, one may purchase records that are related in their musical nature, while proceeding to more highly developed musical compositions. If you are the sort of person who "can't get warmed up" to classical music, you might start your musical adventure with simple melodic waltzes, the more rhythmic types of music, or some of the old favorites. A record library should be so arranged and built that you will be able to derive equal or greater pleasure from purchases made 10 years before. It is highly important to collect records at one's own musical level, keeping an eye and an ear on recordings that are lasting and worthwhile.

An initial group of records can be planned about the Strauss waltzes. These waltzes are frequently admired for their whirling rhythms and lovely melodies, and they seldom fail to captivate the listener. The "Blue Danube" is probably the most popular of all

Strauss waltzes. If one is interested in obtaining a small number of Strauss waltzes, consideration should be given to "De Fledermaus," "The Emperor Waltz," and "Der Zigeunerbaron" ("The Gypsy Baron"). The album called "Johann Strauss: Two Overtures and Two Waltzes" contains some of the best known and best loved of all Strauss music. The "Fledermaus" and "Zigeunerbaron" overtures consist of medleys of tunes from these operettas, each reaching a climax with a waltz.

As you grow in musical taste and discrimination, you will find that Tchaikovsky and Grieg are two composers whose recordings will give considerable pleasure. The waltz from "Serenade for Strings" by Tchaikovsky is a smoothly flowing, highly melodic composition, entirely different from Viennese waltzes, as it is quiet and subdued and the stringed instruments sing forth in a manner that makes it almost irresistible. The other side of this particular record contains an attractive recording by Grieg called "The Last Spring." Some of the more tuneful melodies were never actually composed by a single person; they literally sprang from an entire people, and were handed down vocally from one generation to another as "folk music." In the United States, the best known example stems from southern Negroes, and an excellent recording of this type of music has been made by Columbia.

If, by this time, you feel you are ready for opera, you will find that the two most popular composers are Verdi and Puccini. Both composers wrote melodic arias that attach themselves to one's memory, and you will find yourself before long humming them on your way to your office. The tender passages of "Celeste Aida" will lead you to the robust jovialty of "La donna e mobile." At this point, you should be just about ready for music by a famous French impressionist composer, Claude Debussy. For the most part, Debussy's melodies are comprised of an entirely different texture from those you have been listening to. There is a mysterious, sensitive tone quality about the work of this composer, and it is best to buy his simpler recordings—for example, "Clair de Lune." It would be well to compare the original piano version of "Clair de Lune" with the arrangement for orchestra before choosing a record. The piano impression is more somber.

For an attractive and varied collection of dances, try the album recorded by the Philadelphia Orchestra. "Pops" records will give many hours of delight. The "Russian Sailor's Dance" (from the ballet "The Red Poppy") is a characteristic bent-knee affair that starts off slowly and increases in speed until it winds up in a whirlwind finish. The same 12-measure theme is repeated over and over again, and is varied each time with new tempo and new orchestral coloring.

By now, you should be well on your way to the appreciation and enjoyment of another concept of music. By listening to symphonies in their entirety, one is able eventually to appreciate fully the more advanced interpretation of orchestral repertoire.

A library of records is incomplete without some chamber music. This wonderful form of musical expression has intrigued many physicians, and many, all over the country, have organized groups to play chamber music. An intimacy and completeness surrounds chamber music, and it is a form of music admirably suited to reproduction on the phonograph. Chamber music was originally written for performance in the intimate surroundings of the home. Some people feel cool to this form of music because they probably have listened superficially to some of the more profound compositions without having become familiar with attractive, yet less complicated works. "The Quintet for Clarinet and Strings" by Mozart is filled with delightful melody. The liquid tones of the clarinet blend harmoniously with the two violins, viola, and cello of the string quartet, producing an engaging tonal effect. Once you have become converted to the joys of listening to chamber music, you will find yourself investing in many records of string quartets. If you are a musician in your own right, much pleasure may be derived from accompanying these recordings with your own instrument.

Whether you are interested in music arranged for the concert hall or for the opera, you can sample every type in the quiet of your own home. By the time you have made friends with the majority of classic recordings, you will probably be enough of a musical enthusiast to approach more complex types of music. A library should be built in a planned, musically intelligent fashion. Most persons prefer to acquire a few records at a time, becoming thoroughly acquainted with them through repeated playing. Some like an entire library selected for them; they have a specified amount of money to spend and desire a balanced group of records.

As is true of any collection, a record library requires a certain amount of care. Records should be handled at the edges if possible, as repeated handling of the surfaces will cause records to sound gritty and swishy. Surfaces should be cleaned with a record brush or cloth. The most common ailment of records is warpage. Warped disks can be made flat again by placing them in direct sunlight for five minutes and then placing them, one by one, on a very flat surface under the even weight of several books.

New records should be examined very carefully. They should have a shiny, clean surface, free from scratches, dents, and blemishes. Cracked records should never be played, since the repeated striking of the cracked surface against the point of the needle can damage both needle and pickup arm. Each record requires a certain amount of breaking in; this usually involves no more than playing it all the way through and then dusting it thoroughly with a record brush. As a collection of records grows, storage becomes important. Records should be stored vertically and kept away from direct heat.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Listeria Meningitis, A Report of Eight Cases. J. W. Dedrick. Am. J. M. Sc. **233**:617-621 (June) 1957 [Philadelphia].

Eight patients with listeria meningitis were admitted to the communicable disease unit of the Los Angeles County Hospital within 4 years; 4 died and 4 completely recovered. All received penicillin and sulfonamides, and all but one received chloramphenicol as initial therapy. Sensitivity tests showed organisms from survivors to be responsive in vitro to a larger number of antibiotics than those from patients who died. Afebrility was finally obtained in 2 of the 4 surviving patients after substitution of oxytetracycline for virus-resistant chloramphenicol. The striking morphologic resemblance of listeria monocytogenes to diptheroids and the colonial similiarity on blood agar to beta streptococci have caused many cultures to be either discarded or incorrectly identified, leading many to believe that human listerosis is far less common than it really is. The differentiation of listeria monocytogenes from diptheroids and beta streptococci may be accomplished on the basis of motility, virulence in mice, keratoconjunctivitis in rabbits (diagnostically specific for listeria monocytogenes), and serology. In vitro testing of the variable sensitivities to antibiotics is important in the choice of individual therapy.

Serum Transaminase in Pulmonary Disease and Multiple Infarctions. J. R. Walsh, F. L. Humoller and F. G. Gillick. Ann. Int. Med. **46**:1105-1112 (June) 1957 [Lancaster, Pa.].

Three hundred eighteen determinations of serum transaminase activity were carried out in 112 hospitalized patients, 50 of whom showed evidence of myocardial infarction. These determinations were made with the aid of Karmen's spectrophotometric method in an attempt to determine the specificity of the serum transaminase test in patients with myocardial infarction. While increased serum transaminase levels were found most commonly in patients with acute myocardial infarction, elevated levels also were found often enough in patients with necrosis and infarction of other organs to suggest caution in interpretation. The highest values of 500 units or more of serum transaminase activity were found in patients with multiple pulmonary and renal infarcts. The typical curve for the time course of serum transaminase levels of myocardial infarction also was observed in patients with multiple pulmonary and renal infarcts. In patients with pulmonary infarction, increased serum transaminase levels ranging from 40 to 100 units were observed, particularly after the 4th day. In certain cases the increased serum transaminase level became evident between the 6th hour and 5th day, exactly as in patients with myocardial infarction. These observations definitely reduce the usefulness of the test for the differentiation of myocardial from pulmonary infarction. The occurrence of serum transaminase levels of more than 100 units, however, was rare in patients with pulmonary disease. There were only 2 such cases among the 112 patients. A value of 186 units was recorded in 1 patient with fulminating pneumonia and a value of 104 units in a patient with pulmonary infarction. Increased values of more than 40 units of serum transaminase activity were observed in patients with pulmonary infarction, multiple infarctions, pneumonia, carcinoma of the liver, pancreatitis, trauma, and cirrhosis of the liver and in 1 patient with uremia.

Clinical Manifestations of Hypopotassemia. B. Surawicz, H. A. Braun, W. B. Crum and others. Am. J. M. Sc. **233**:603-615 (June) 1957 [Philadelphia].

Patients with abnormally low concentrations of plasma potassium may have numerous functional and anatomic derangements. However, the majority of the signs and symptoms related to hypopotassemia are nonspecific, being found in many severely ill persons without low potassium levels. Multiple disturbances of homeostasis complicate potassium deficiency, obscuring and modifying its effects. The incidence of hypopotassemia among females was significantly higher than in males. The mortality rate of hypopotassemia patients was much higher than the over-all hospital rate. Hypochloremic alkalosis with hypocalcemia commonly accompanied patassium deficit. Anorexia, nausea, and vomiting are part of the clinical symp-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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tomatology, which included inactivity of the deep tendon reflexes as the only factor correlated with potassium deficit. A rough correlation exists between impairment of intestinal peristalsis and degree of potassium deficit. The most significant changes accompanying rapid infusion of potassium were increased peristaltic activity and improved mental status. The nonspecific nature of clinical manifestations of hypopotassemia emphasizes the importance of the electrocardiogram, the electromyogram, and other laboratory aids in the diagnosis of this disorder.

Molecular Diseases of Hemoglobin: I. Introduction and Incidence. T. P. Haynie, H. L. Dobson and R. A. Hettig. Ann. Int. Med. **46**:1031-1038 (June) 1957 [Lancaster, Pa.].

The incidence of abnormal hemoglobins was studied by the authors with the aid of paper electrophoresis in 350 white and 400 Negro patients at the Jefferson Davis Hospital, in Houston, Texas. The results obtained were compared with those obtained by Smith and Conley in 500 white and 500 Negro patients at the Johns Hopkins Hospital and by Schneider in 60 white and 505 Negro blood bank donors at the John Sealy Hospital in Galveston. The authors' study and that of Smith and Conley, representing the incidence in general hospital populations, agreed quite well. The study by Schneider differed in that persons with known hemoglobin disease did not appear in this series, which was based on blood bank donors, since persons with overt hemolytic disease or anemia were not permitted to donate blood. Persons with asymptomatic trait abnormalities, however, were included, and Schneider's statistics thus provided a good indication of the incidence of trait abnormalities in a population considered to be normal.

Abnormal hemoglobins were not found in any of the 910 white persons screened by electrophoresis in the 3 studies. In the 1,405 Negroes, there was an incidence of 11.5% of abnormal hemoglobins as detected by electrophoresis. S hemoglobin was present in 9.4% and C in 2.2% of the Negroes. Only 1 case of homozygous C disease was detected in the 3 series. The incidence of the sickle trait varied from 7.2% to 11.3% in the 3 series, with a mean of 8.4%, thereby providing essential agreement of trait incidence between electrophoretic techniques and those based on the findings of in vitro sickling reported by other workers. The figures from all 3 series combined agreed quite well with the notion that about 10% of the Negro population has sickle cells in the peripheral blood and that 10% of this group has sickle cell anemia.

Filter-paper electrophoresis is the best single method for the detection of molecular diseases of hemoglobin. This method will separate all but combinations of A, F, and G hemoglobins and combinations of S and D hemoglobins. The most common abnormal hemoglobin is S, while C is observed less frequently. The diseases observed were trait, homozygous disease, and double heterozygous disease. The incidence of molecular disease of hemoglobin in Negroes is about 11.5%.

SURGERY

Cerebral Damage After Metatraumatic Ligation of Carotid Artery. U. Venzlaff and E. Trostdorf. Beitr. klin. Chir. **194**:328-349 (No. 3) 1957 (In German) [Munich, Germany].

Ligation of the carotid artery was performed after injuries involving the carotid artery in 16 patients. In 15 patients these injuries were sustained during World War I and in 1 patient in a traffic accident. Ligation of the common carotid artery was performed in 10 patients; ligation of the common carotid and internal carotid arteries in 3; and ligation of the internal carotid artery, of the internal and external carotid arteries, and of the external carotid artery in 1 each. Ligation was done on the left side in 11 patients and on the right side in 5. Complete contralateral pyramidal hemiplegia resulted immediately or within 2 hours to 5 days in 11 of the 16 patients; it was permanent in 7, and one of the 4 patients who gradually improved made a complete recovery. Two additional patients had symptoms of latent hemiplegia, such as abnormal reflexes and mild dysdiadochokinesia. Only 3 patients did not have any pyramidal signs. All the patients with pyramidal hemiplegia also showed signs of involvement of the corticobulbar tracks. Of 8 patients with pyramidal hemiplegia resulting from ligation of the carotid artery on the left side, 7 had aphasic disturbances of speech. Motor aphasia was predominant. The most severe and refractory disturbances of speech were observed in 3 patients over 25 years of age with combined motor-sensory aphasia. Gradual improvement resulted in the other patients. Weakness in writing and reading occurred in 3 patients. Blindness on the side of the focus resulted from atrophy of the optic nerve in 1 patient. The atrophy may have been caused by spasm or embolism of the central retinal artery blocking the circulation.

There was a constant relationship between the extent of the psychic disturbances and the severity of the neurological deficiencies. Psychic disturbances were more severe in older patients and in those with ligation at the left side. Of the 5 patients with ligation at the right side, only the oldest, a 39-year-old man, had affective disturbances of regulation, slowing down, and a tendency to depression. Of 11 patients with ligation on the left side, 9 had severe psychic disturbances, including mental deterioration, character changes, and functional weakness of the brain. Only the 2 youngest patients, who had been operated on at the age of 20 years, were free from psychic disturbances.

Late complications were observed after free intervals of from 1 to 9 years. Headache, vertigo, tendency to collapse, and sweating were observed in 4 patients

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who first did not have any encephalopathic complaints after the operation. These complaints became gradually worse, and functional weakness of the brain developed in 2 patients whose memory and concentration weakened. Symptomatic epilepsy occurred as a late complication in 4 patients, and a decrease in libido and potency in 1 patient. Nine years after the ligation 1 patient had sudden attacks of feeling of annihilation, vertigo, blackout, and temporary worsening of his residual paresis in the right arm. These observations show that ligation of the carotid artery is endured only in very rare cases without causing a deficiency in the blood circulation of the brain which may, occasionally, develop only years after the operation.

Direct Vision Repair of Intracardiac Defects Utilizing a Rotating Disc Reservoir-Oxygenator. F. S. Cross and E. B. Kay. Surg. Gynec. & Obst. **104**:711-716 (June) 1957 [Chicago].

Many pump-oxygenator systems have been devised for intracardiac operations for the repair of congenital cardiac anomalies. The basic mechanism of the rotating disk reservoir oxygenator, used in the 45 patients operated on for intracardiac defects during the first 10 months of 1956, is a series of 59 silicone-coated stainless steel disks supported horizontally in a pyrex cylinder coated with silicone resin. Blood introduced at one end of the cylinder is removed from the bottom of the opposite end. The rotation of the disks prevents the channeling of blood along the bottom of the cylinder. With the oxygenator primed with 1,400 cc. of whole blood and the disks rotating at a rate of 120 rpm, there is an exposure area of 108 sq. m. per minute. A mixture of oxygen and 1.5% carbon dioxide, warmed in a sand bath heated by an electric mantle, is supplied. Continuous monitoring of central venous pressure and maintaining it at the preperfusion level constituted the greatest aid in achieving a balanced perfusion during the periods of cardiac bypass. Any unmeasured extrinsic blood loss or reflex vasodilatation resulting in decreased venous return to the cavae and a concomitant decrease in the venous return to the oxygenator automatically is compensated for with blood from the reservoir-oxygenator and is measured as a fall in the oxygenator blood level. In this way the central venous pressure acts as a fairly accurate index of the circulating blood volume in the patient. After cardiotomy closure the caval tapes are released and the pump rate decreased slowly, with a satisfactory central venous pressure and systemic arterial pressure maintained until the heart takes over satisfactorily. The patient is weighed immediately postoperatively, and the weight is adjusted by means of blood transfusions or blood removal if necessary.

The greatest experience to date with the intracardiac repair techniques has been with ventricular septal defects, atrial septal defects, and pulmonic stenosis, alone or in various combinations. Ivalon sponge prostheses have been used in the repair of the larger ventricular septal defects, whereas the smaller defects have been closed by interrupted sutures of 000 silk. Atrial septal defects have been closed by direct suture by use of either interrupted sutures of 000 silk or a continuous suture reinforced with interrupted sutures. Thirty-three of the 45 patients survived the operation. No deaths could be ascribed to the use of the pump oxygenator. Pulmonary complications were the most frequent postoperative problem. There can be little doubt that the future of cardiac surgery lies in the further development of safe direct-vision techniques. The advantages of the open techniques are (1) easy visualization of all valves, septums, and chambers; (2) complete correction of existing defects when possible; and (3) identification and repair of associated defects previously undiagnosed. Where there has been an opportunity to compare open techniques with previously tried closed techniques, the former have proved more satisfactory from all standpoints. Emphasis is placed on the use of extensive physiological studies before, during, and after the period of cardiac bypass, for it has been through these studies that the techniques of surgery under direct vision have been improved. A satisfactory pump-oxygenator is only part of the formula of success.

Surgical Repair of Ruptured Interventricular Septum Following Acute Myocardial Infarction. D. A. Cooley, B. A. Belmonte, L. B. Zeis and S. Schnue. Surgery **41**:930-936 (June) 1957 [St. Louis].

Rupture of the interventricular septum resulting from or secondary to myocardial infarction is widely recognized as a fatal complication of acute coronary occlusion. Septal rupture occurs approximately 7 days after acute infarction, with death resulting from rapidly progressive cardiac decompensation. A loud precordial systolic murmur appearing after a coronary occlusion is of diagnostic significance, as emphasis is placed on early diagnosis, vigorous treatment of cardiac decompensation, and prompt preparation for operation within the time interval (several hours or days) between septal rupture and ultimate cardiac failure. Diagnosis may or may not be confirmed by catheterization. Direct surgical correction of this defect and other serious complications of acute myocardial infarction, such as ventricular rupture with pericardial tamponade, ventricular aneurysm, and ruptured papillary muscle, is now feasible with the use of temporary extracorporeal circulation.

Pericardial Fat Necrosis: Report of 3 Cases. R. C. Jackson, O. T. Clagett and J. R. McDonald. J. Thoracic Surg. **33**:723-729 (June) 1957 [St. Louis].

The authors report on 3 patients, 2 men aged 52 and 63 years, respectively, and 1 47-year-old woman with pericardial fat necrosis. Each patient was quite

obese, and this was probably a prerequisite of their disease. All patients presented clinically with acute low anterior chest pain, and the roentgenograms of the chest showed a mass close to the cardiac shadow. All patients had a pleuritic component to their pain at some phase of the illness, and in 2 it was referred to the shoulder. In general, symptoms persisted to become chronic, although intermittent in character. Thoracotomy was performed, with resection of the diseased tissue. Histologically, the surgical specimens showed the usual appearance of fat necrosis and, in addition, abnormalities of some of the blood vessels such as a severe degree of subintimal fibrosis and a mild to moderate medial hypertrophy with consequent narrowing of the lumens. Similar vascular changes were found in 6 of 11 surgical specimens of fat necrosis of the breast and in 4 of 6 surgically removed specimens of epiploic appendices, and are believed to be secondary in nature. The reported 3 cases represent a previously undescribed clinicopathological entity.

Comparative Experimental Study of Aortic Grafts. H. B. Shumaker, H. Kajikuri, P. Grice and others. Surgery **41**:943-957 (June) 1957 [St. Louis].

Clinical and experimental studies have demostrated that a variety of plastic materials can be used for replacement of arterial segments. In this study 9 types of grafts were used: (1) homografts, (2) washed nylon filter fabric, (3) unwashed nylon filter fabric, (4) braided nylon tubular graft, (5) nylon-polythene-nylon, (6) nylon-polythene, (7) Vinyon-N, (8) pig heterografts, and (9) cow heterografts. These grafts were implanted in the thoracic aorta as a replacement for a previously removed 5-cm. segment. Observed grafts were adjudged on the basis of patency, condition of inner lining, presence of intramural thrombi, degenerative changes, and external clotting and constriction. The best results were obtained with the nylon washed filter fabric, braided tubular nylon, and homografts. The poorest results were obtained with the nylon-polythene, Vinyon-N, and heterografts respectively. Although no one of the plastic grafts was as amenable to suturing to the ends of the aorta as the homograft, there was no real difficulty encountered in joining the plastic graft to the aortic host. The author concludes that small-diameter grafts of filtered or braided nylon treated with formic acid and silicon are quite satisfactory as canine aortic prostheses and possibly superior to freeze-dried homografts.

Lobectomy for Pulmonary Tuberculosis: An Analysis of 301 Cases. V. O. Björk. J. Thoracic Surg. **33**:754-769 (June) 1957 [St. Louis].

Three hundred one patients, 170 male and 131 female, between the ages of 10 and 69 years, with pulmonary tuberculosis that was bilateral in 146 (48.5%), underwent lobectomy. Ten patients died. Death resulted from the operation in 7, an operative mortality of 2.3%, although patients with ventilatory insufficiency were accepted for operation. One hundred sixty-three patients were followed up for 1 to 5 years. Cavitary tuberculosis was the most common indication for lobectomy in 255 patients (85%). The right upper lobe was the most common localization. Bronchial stenosis was the indication for resection in 26 patients (9%), bronchiectasis with positive sputum in 6, tuberculous pneumonia in 6, tuberculous empyema with bronchial fistula in 7, and a secondary infected congenital cyst in 1. A space-diminishing procedure was added to the resection in only 18 patients. In the beginning a 3-rib thoracoplasty was performed in 33 patients (11%) or a 5-rib thoracoplasty in 14 patients (5%), and after a few months up to 1 year later, resection was performed with additional rib resection if considered necessary. Later on a one-stage operation always was used. To avoid the immediate danger of paradoxical movements of the chest wall with carbon dioxide retention and the late hazards of infection in a foreign body, an osteoplastic thoracoplasty was devised with fixation of the posterior parts of the ribs by nylon sutures through drill holes; this procedure was added to a lobectomy in 149 patients.

Gratifying results were obtained; 160 (98%) of the 163 patients gave a negative direct smear, and a negative culture and negative results from a guinea pig test were obtained from sputums and gastric washings of 138 patients (85%). One hundred twenty-nine patients (79%) were working full time. The osteoplastic thoracoplasty gave a much better cosmetic result and better arm movements than a thoracoplasty with rib resection. There was, however, a higher incidence of postoperative pain, i. e., 20%, instead of 13% in the group of patients who had rib resection. The late functional result was very good after resection with a space-diminishing procedure. There was usually no significant decrease of the oxygen uptake or ventilation on the operated side after a resection, although there was a significant decrease of the maximal breathing capacity. The contralateral side withstood the resection very well.

Aberrant Pulmonary Artery with Intralobar Sequestration. A. E. Anderson, J. B. Brown and C. B. Roesch. Ann. Int. Med. **46**:1092-1098 (June) 1957 [Lancaster, Pa.].

The authors report the occurrence of an aberrant pulmonary artery with intralobar sequestration, a developmental defect of the lungs which is generally considered to be rare, in a 21-year-old man and in a 13-year-old boy. In the first patient, the anomalous artery arose from the abdominal aorta and supplied a cystic mass in the posterior part of the left lower lobe. The location of the sequestrated mass in this patient was the same as that in earlier reports. In the second patient, a sequestrated segment of the right upper lobe was joined to the right subclavian actery by several large trunks. It was considered as a different variety

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of the same fundamental defect, differing only in location. A similar case was not found in the literature. With Pryce's concept of developmental traction on attached lung in mind, aberrant vessels from subclavian arteries would be expected to be associated with sequestration in some patients, as is seen with pulmonary arteries elsewhere arising from the aorta or its branches. The pattern that occurred in the boy must be a rarity, although it is not inconsistent with the theory.

In most cases of aberrant arteries with sequestration, venous drainage takes place by way of the normal pulmonary venous system. Secondary infection usually produces symptoms at an early age. Hence the condition is frequently diagnosed as recurrent pneumonia, empyema, abscess, or bronchiectasis. Chronicity and recurrences occasionally require surgical intervention. In such situations, particularly in the presence of lower lobe masses and cystic lesions, awareness of the possibility of anomalous vessels may prevent serious hemorrhage at operation. In a few patients reported on previously in whom the suspicion was strong, the diagnosis has been established preoperatively with the aid of planograms and aortography, but as a rule the correct diagnosis has been established by thoracotomy. Surgical excision is usually curative.

An Appraisal of One Stage Anterior Resection in Diverticulitis of the Sigmoid Colon. J. M. Waugh and A. J. Walt. Surg. Gynec. & Obst. **104**:690-698 (June) 1957 [Chicago].

The surgical treatment of diverticulitis of the sigmoid and descending colon has undergone a decided change in the past decade. The authors demonstrate this on the basis of 320 operations performed for this condition at the Mayo Clinic between 1945 and 1954. The numbers of patients undergoing one-stage and multiple-stage anterior resection or obstructive resection or several other operations are listed and the procedures are defined. There has been a noticeable trend toward the more frequent application of one-stage resection, with primary anastomosis but without colostomy. Antibiotic therapy has been largely responsible for this fact by aiding resolution of the inflammatory process in the acute phase and consequently making elective surgery, with a reduced mortality rate, possible. Ninety-three of the 320 operations were one-stage resections with primary anastomosis. The main purpose of this study was to appraise the clinical features and operative results in this group of 93 patients against the background of the remaining 227 patients for whom various different procedures were felt to be indicated. Postoperative difficulties were few, the hospital stay averaged 16 days, there have been no known recurrences, and the single death which occurred was not related to the operation. There has been a steady increase in the percentage of patients regarded as suitable for this type of operation. This is in part attributable to a deliberate effort to advise elective resection before the onset of complications has made a single-stage operation unfeasible. The authors make a plea for earlier recognition of those patients who subsequently will require operation. Advances in colonic surgery justify a less conservative attitude than has heretofore prevailed.

Another factor accounting for this increase in one-stage resections has been the recognition that this procedure can be performed safely in certain cases in which there is persistent inflammation and established fistulas. The old rigid criteria, which decreed that the presence of obstruction of even minor degree, fistula, or localized active peritonitis automatically demands a preliminary defunctioning colostomy, are no longer tenable. The situation should be judged in each case by the pathological process at the time of laparotomy. The primary treatment of diverticulitis remains medical; about 80% of the patients will respond satisfactorily. The rest will require resection. For those who require operation urgently or in whom the inflammatory process is unduly acute or extensive, the desirability of a multiple-stage operation remains unchallenged. It is among the remainder that the one-stage operation has been shown to be applicable, in the majority of cases, with the promise of most satisfactory results.

NEUROLOGY & PSYCHIATRY

Histopathology of Psychomotor Epilepsy: A Study with Silver Carbonate. K. Scharenberg. A. M. A. Arch. Neurol. & Psychiat. **77**:595-604 (June) 1957 [Chicago].

The investigation is based on human biopsy material from the temporal lobes of 60 patients with psychomotor epilepsy. Forty-five of these were placed at the author's disposal by Dr. Percival Bailey, and the remaining 15 were treated in the University of Michigan Hospital or were obtained from other sources. The silver carbonate method of del Rio Hortega revealed extensive destruction of the gray and the white matter of the temporal lobes. In the gray matter the neurons and their auxiliary systems of glia were affected, and there were numerous areas of necrosis. In the white matter ameboid degeneration of glia was the dominant change.

Myasthenia: II. Physiopathology, Diagnosis, Treatment. J. Cambier. Presse méd. **65**:737-740 (April 20) 1957 (In French) [Paris].

The basic disorder in the myasthenic syndrome is a disturbance in neuromuscular transmission. The exact nature of this disturbance, however, has not been fully established; in particular, the connections between myasthenia and changes in the thymus and between myasthenia and the patient's endocrine state have not been explained. The remarkable responsiveness of the myasthenic syndrome to anticholinesterase drugs

shows that the block in neuromuscular transmission is the result of inadequate, rather than irreversible, depolarization of the motor plate. Experimental findings obtained by various workers warrant the conclusion that the myasthenic block is a competitive block produced by the choline which is normally set free when acetylcholine is hydrolyzed. Such a process would account well for the principal characteristic of the myasthenic disturbance, which is fatigability caused by the appearance or aggravation of the block under the influence of effort. It has not yet been possible, however, to determine whether the anomalous behavior of the myasthenic muscle is due to an abnormal response of the motor plate to the choline itself or whether it results from the formation in myasthenic patients of a choline derivative that exerts a competitive action, in relation to acetylcholine, on a normal motor plate. Progress has undoubtedly been made in determining the physiopathological nature of the muscular disturbance in myasthenia, but its underlying cause is still unknown. The frequency with which changes are found in the thymus and the undeniable influence of widely differing endocrine factors strongly suggest that the functional disturbance at the neuromuscular junction is not primary but rather secondary to a disease that affects the organism as a whole.

A diagnosis of myasthenia should be considered whenever a patient presents an isolated impairment of the extrinsic muscles of the eye. Difficulties are sometimes encountered, but they can usually be resolved by the prostigmin test. Various neuromuscular conditions in which fatigue is an aggravating factor and there is a certain sensitivity to prostigmin, and various transient myasthenic syndromes appearing after infection or intoxication, must also be distinguished from genuine myasthenia gravis.

Palliative medical measures designed to relieve the myasthenic block constitute the most effective treatment yet available, although some successes have been secured with thymectomy or carotid sinus enervation. Therapeutic trials of corticotropin (ACTH) and cortisone have produced highly discordant results: thus cortisone is incapable of bringing about a remission and may prove aggravating. The use of corticotropin, on the other hand, sometimes leads to improvement, but the improvement is often preceded by a temporary aggravation, and fatal complications have even been reported in some cases. The principal problem connected with the use of corticotropin concerns not so much its effect, which is undeniable, as the mechanism by which that effect, whether good or bad, is produced. Prostigmin and the newer preparations, pyridostigmin (Mestinon), edrophonium (Tensilon), and Win 8077 (Mysuran), are the anticholinesterase drugs now being used for the relief of myasthenic symptoms. The dosage varies from patient to patient and even from time to time in the same patient. Overdosage must be carefully avoided because it may lead to dangerous respiratory crises. Anticholinesterase drugs have greatly improved the condition of patients with myasthenia, but they do not seem to have any effect on the course of the disease. Myasthenic patients should therefore be advised to avoid intense or prolonged physical exertion, and they must learn to recognize the circumstances in which their therapeutic needs are increased, e. g., during an infectious illness, pregnancy, or menstruation. They should, in fact, be given information comparable to that given diabetic patients using insulin.

Neurological Complications of Rubeola (Measles). H. R. Tyler. Medicine **36**:147-167 (May) 1957 [Baltimore].

Neurological complications developed in 85 patients with measles who were recorded at the Johns Hopkins and Baltimore City hospitals between 1919 and 1956. The authors review observations on 67 of these patients. The neurological complications associated with measles may be separated into four major groups: (1) a diffuse encephalomyelopathy characterized by perivascular demyelination and perivenous microglial proliferation, (2) infarctions in the distribution of major arterial channels, (3) acute cerebral edema often associated with some mild vascular changes and neuronal changes, and (4) rarer complications (e. g., retrobulbar neuritis, toxic psychosis, and sinus thrombosis). Some confusion has arisen in the literature because of the attempt to consider each of the complications of measles as "encephalitis." It is believed that the term should be restricted to that illness which has the diffuse disseminated demyelinating process as its basis. The clinical picture associated with such pathological changes may vary from a mild delirium or a single convulsion to a deep coma with or without focal signs. These represent a continuous spectrum, and the symptoms vary in terms of the severity of the pathological process and the tendency for it to be more severe in certain areas, i. e., giving more cerebellar signs in one patient, more myelitic signs in another. The important point to note is not the focal signs as such but the presence of abnormalities elsewhere in the neural axis, i. e., minimal mental changes in association with the myelitis, behavioral and personality changes in the presence of cerebellar signs. Electroencephalography may be of help in suggesting the diffuseness of the process. The spinal fluid almost always is under normal pressure, and the presence of a lymphocytic cellular reaction or raised protein was present in over 89% of the cases in this series.

The second group—the infarctions in the distribution of the major arterial channels—is represented clinically by the acute hemiplegias. These can be distinguished from the first group by their onset at an earlier age, their lack of time relationship to the rash, the permanency of the hemiplegia, and the high incidence of seizures. The patients with acute cerebral edema or "toxic encephalopathy" are acutely ill individuals. They present the signs of acutely increased intracranial pressure. Papilledema is marked. Most often there is a profound disturbance of mental status, and

most neurological signs are probably on the basis of the swollen hemispheres displacing the mesial portions of the temporal lobe down through the tentorium and compressing the brain stem. The isolated cases of retrobulbar neuritis, without any evidence of the involvement of the rest of the nervous system, were felt to be on a different pathological basis from the encephalomyelitides. The usual measles encephalomyelitis is not fatal per se; the convulsive disorder causes most of the fatalities. If this can be controlled the prognosis is excellent. In terms of recovery, the worst prognosis appears to be in infants; none followed by the authors emerged unscathed. However, time has a tendency to bring improvement. The behavioral disorder often seen after the illness usually disappears, provided that the patient's IQ remains normal; with a low IQ the prognosis is poor for behavioral improvement. Convulsive disorders may occur a number of years after measles encephalomyelitis. The infantile hemiplegias usually resulting from vascular infarction tend to be permanent, and seizures often develop in later years. "Toxic encephalopathy" has a high mortality.

Some Features of Cerebellar Metastases of Cancer of Lung. G. J. Fernández, F. Muxí and J. Folle. An. Fac. med. Montevideo **41**:251-374 (Nov.-Dec.) 1956 (In Spanish) [Montevideo, Uruguay].

Neurological disorders appearing in the course of visceral cancer are due to either cerebellar metastases or to local foci of inflammation, ischemia, or degeneration of certain cerebellar zones without metastases. In rare cases, the cerebellar metastases of visceral cancer may follow their course without producing either neurological symptoms or symptoms of intracranial hypertension. The author reports the following case: A man 71 years old complained of bronchopulmonary symptoms of about one year's duration and of dizziness, occasional headache, and occasional spitting of blood. Pulmonary tuberculosis was ruled out. A diagnosis of bronchopulmonary cancer was made by a roentgen examination of the chest and by bronchography. No brain lesion could be roentgenologically visualized. With the exception of dizziness and an occasional headache, neither symptoms nor ocular changes of intracranial hypertension were observed. The cerebrospinal fluid was normal. The patient refused an operation. He suddenly became very ill with an infection and died two years later. Partial autopsy showed a Malphigian epithelioma of the left upper bronchus, which involved all of the upper lobe of the lung and the left pulmonary vein and the atrium. A metastasic growth, 5 cm. in diameter, was present in the left cerebellar hemisphere and caused the vermis to be displaced to the right. The metastasis could be ennucleated from the nervous tissue, which was not infiltrated. The authors advise the making of clinical and roentgen examinations of the chest for bronchopulmonary cancer in all cases of cerebellar symptoms, even if the symptoms are mild.

GYNECOLOGY & OBSTETRICS

The Prognostic Significance of Glandular Involvement in Cold Knife Conization Biopsies in Carcinoma in Situ of the Uterine Cervix: An Analysis of 136 Cases. W. S. Baker Jr. and B. L. Hawks. Am. J. Obst. & Gynec. **73**:1266-1276 (June) 1957 [St. Louis].

One hundred thirty-six women between the ages of 21 and 58 years with microscopic evidence of carcinoma of the uterine cervix but without invasion of the underlying stroma (cancer in situ) were studied to determine the possible prognostic significance of cervical glandular involvement in in situ tumor in the pretreatment conization biopsies. One hundred thirty conization biopsies were performed before the institution of any definitive therapy. Forty-five patients (34.7%) were observed to have involvement of the endocervical glands; the conization biopsies gave negative results in 10 (7.6%) and positive results for cancer in situ without involvement of glands in 75 (57.7%). After the diagnosis was established, 132 patients were operated on or were given combined surgical and irradiation treatment. Thirty-six (27.3%) of the 132 patients were found to harbor residual tumor in the postoperative specimens and 96 did not. The pretreatment conization biopsies obtained from 14 or 38.8% of the patients with residual tumor in the postoperative specimens belonged to the group of 45 conization biopsies with endocervical glandular involvement, for an incidence of 31.1%. The preoperative conization biopsies obtained from the remaining 22 patients with residual tumor in the postoperative specimens belonged to the group of 75 conization biopsies without involvement of the endocervical glands, for an incidence of 29.3%.

Sixty-three patients (or 46.4% of the 136) were adequately followed since being treated, and 73 were lost to follow-up over a period of 7 years. Twenty-one patients, or 15.4% of the combined groups, were free of recurrence over 5 years. Fourteen, or 18.8% of the 75 patients without involvement of the endocervical glands in the conization biopsies, were followed for 5 years without recurrence of disease, and 4, or 8.8% of the 45 with glandular involvement in the conization biopsies, attained the 5-year salvage mark safely. Fifteen, or 15.6% of the 96 patients without residual tumor in the postoperative specimens were followed for 5 years without recurrence of disease and 6, or 16.6% of the 36 with residual disease in the postoperative specimens were also followed uneventfully for a 5-year period. Six patients had extensive glandular involvement in their conization biopsies and no involvement of glands in the preceding quadrant biopsies, thus showing a progression of the disease miscroscopically. Both cases of invasive cancer of the cervix diagnosed in the postoperative specimens were preceded by extensive endocervical glandular involvement in the cones. There were 3 cases of residual tumor in the postoperative specimen that were pre-

ceded by conization biopsies negative for evidence of cancer. There were no deaths to date that could be attributed to carcinoma in situ of the uterine cervix.

The diagnosis of cancer in situ is possible only if the 360-degree cold-knife conization biopsy technique is carried out in every patient with suspected cervical malignancy. Total hysterectomy and resection of a generous vaginal cuff with preservation of normal-appearing ovaries in all women aged less than 45 years is the treatment of choice in those with a conization biopsy positive for cancer in situ of the uterine cervix. Any other form of therapy is considered inadequate, as evidenced by the high incidence of residual tumors noted in this series. The presence of glandular involvement in the conization biopsies did not appear to affect adversely the prognosis over a 5-year period nor to increase materially the incidence of residual tumor in the postoperative specimen. Extensive glandular involvement by noninvasive cancer in the conization biopsy is considered to be a more advanced stage of the disease from the standpoint of microscopic pathology but it does not constitute invasion of the underlying stroma nor adversely affect long-range prognosis in any patient. The incidence of residual tumor in this series is thought to be due to incomplete removal of the tumor by conization biopsy, to its possible multicentric origin, or to a combination of both, and not to involvement of the endocervical glands.

Carcinoma of the Vulva. J. H. Isaacs and N. H. Topek. Am. J. Obst. & Gynec. 73:1277-1285 (June) 1957 [St. Louis].

Of 41 women with carcinoma of the vulva seen in the course of 17 years, 18 (43.9%) were seen during the last 5 years. These data suggest that with the over-all increase in life expectancy there has been a concomitant rise in the incidence of vulvar malignancy. Six of 16 patients who were followed up for 5 years or more were living and well, a 5-year survival rate of 37.5%. This result was due to inadequate therapy employed in some of the earlier cases. Of 11 patients adequately treated either by radical valvulectomy and irradiation or by radical valvulectomy and lymphadenectomy, 6 survived for 5 years, a survival rate of 54.5%, which approaches an acceptable percentage.

A critical survey of the symptomatology of the patients with carcinoma of the vulva indicates that it is a disease of older women and of slow development, and that chronic irritative lesions of the vulva are predisposing factors. Such precancerous lesions must therefore be excised. Patients with coexistent carcinoma of the vulva and veneral granuloma generally have a better prognosis, since the accompanying inflammatory adenitis blocks the lymphatic pathways, preventing metastases. When vulvectomy is done for precancerous lesions, the specimen must be cut for multiple section study, as previously undetected malignancy may be found. If discovered, then bilateral groin dissection is essential. Radical surgery is the only means of increasing the 5-year cure rate. The extent of the surgery will depend on the condition of the patient and the extent of the disease. A 1-stage procedure including radical node dissection and vulvectomy as advocated by other workers is ideal but the reported 12% operative mortality suggests 2-stage or even 3-stage operations may be best in poor-risk patients. The exenteration operation advocated for the treatment of patients with far-advanced disease involving the intestines and/or the bladder resulted in an alarmingly high operative mortality of 45%, which makes this method not yet practical.

OPHTHALMOLOGY

The Treatment of Retinoblastoma by Radiation and Triethylene Melamine. A. B. Reese, G. A. Hyman, G. R. Merriam Jr. and A. W. Forrest. Am. J. Ophth. 43:865-871 (June) 1957 [Chicago].

The treatment of retinoblastoma by combination of x-radiation and triethylene melamine is more effective than treatment by x-radiation alone. Results of the combined treatment are more favorable from a standpoint both of vision restored and of minimal time lapse from commencement of treatment. TEM employed intramuscularly, either by itself or in combination with x-radiation, is more effective than when employed orally, due to emesis, irregularity of absorption, and resultant interference with dosage. The lower dosage of x-radiation now required in the combined treatment has led to no vitreous hemorrhages such as are encountered with the dosage required in deformities. Multicentricity of foci did not affect the cure rate in either group. A failure of the combined group in lesions of 5 disk diameters or less was rare, while in lesions greater than 8 disk diameters there were failures by both methods. Use of TEM intra-arterially is indicated as being most effective. This method is used to increase many fold the amount of drug reaching the tumor when the tumor is large and enucleation not possible, when there are tumor cells present at the cut end of the optic nerve at enucleation, and in orbital recurrence following prior enucleation.

Use and Misuse of Acetazoleamide (Diamox) in the Treatment of Glaucoma. P. A. Chandler. A. M. A. Arch. Ophth. 57:639-643 (May) 1957 [Chicago].

The use of acetazolamide (Diamox) has been widespread in the treatment of glaucoma, since this carbonic anhydrase inhibiting drug has a pressure-lowering effect. But this is due solely to a lessening of the rate of aqueous humor production. The obstruction to outflow of aqueous humor is not influenced by the drug. Treatment of glaucoma by the use of Diamox must be, therefore, regarded as a palliative one. It is often of great value in preventing damage to vision, while other measures are employed to relieve the fundamental difficulty: obstruction to outflow of

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aqueous humor. The greatest field of usefulness of the drug is in the treatment of secondary glaucoma, which is, by definition, a rise in ocular tension secondary to some other eye disease. If the fundamental disease can be cured, secondary glaucoma is likewise cured. Diamox appeared to be of great value as a substitute for palliative operations. There is no contraindication to its use, except for the unpleasant side-effects experienced by some patients.

The situation is quite different in patients with angle-closure glaucoma, since the obstruction of outflow is due to closure of the angle. In the early stages a simple surgical procedure effects a complete cure of the disease, whereas it is well recognized that in the late stages all treatment may fail. If Diamox, therefore, is employed along with miotics in the treatment of angle-closure glaucoma, the level of tension is no longer a guide as to the extent of closure of the angle. The drug should never be used as a continuing treatment in any form of angle-closure glaucoma, but, once operation is decided on, Diamox serves a very useful purpose as an immediate preoperative treatment in all types and stages of angle-closure glaucoma. No contraindication to the use of the drug is given when there is the question of controlling the residual increased tension.

Report of a New Carbonic Anhydrase Inhibitor (Squibb-MC-9367). M. H. Balistocky and B. C. Gettes. Am. J. Ophth. 43:730-735 (May) 1957 [Chicago].

A single dose of 500 mg. of a propanyl derivative of acetazolamide (Diamox), known as Squibb N (5-sulfamoyl-1,3,4-thiadiazole-2-YL) propionamide, or MC-9367, was given orally to 30 patients with 43 glaucomatous eyes. Of the 43 eyes the glaucoma was of narrow-angle type in 13, wide-angle type in 19, aphakic in 5, secondary to uveitis in 2, secondary to vascular occlusion in 1, secondary to a dislocated lens in 2, and secondary to intumescent cataract in 1. Twenty-three patients with 40 nonglaucomatous eyes were used as controls and were likewise given a single dose of 500 mg. of MC-9367 orally after their intraocular pressures had been recorded. Decreases of 6 mm. Hg or more in the intraocular pressure were considered significant and were observed in 18 eyes of the patients in the control group. None of these patients was receiving miotic therapy.

MC-9367, when combined with the usual miotic drugs, was effective in reducing the intraocular pressure in all 13 eyes with narrow-angle glaucoma, in 16 of the 19 with wide-angle glaucoma, in 3 of 5 with aphakic glaucoma, in the 2 with glaucoma secondary to uveitis, in the 2 with glaucoma due to bilateral dislocated lens, and in the eye with glaucoma secondary to an intumescent cataract. MC-9367 was ineffective in the eye with glaucoma due to vascular occlusion. In no case in which Diamox had failed was MC-9367 effective. The greatest period of effectivity of MC-9367 was from 2 to 4 hours after its administration. None of the patients reported any paresthesias, and no toxic effects were noted after a single dose of the drug. MC-9367 given in a single dose orally is an effective agent in lowering the intraocular pressure in man.

THERAPEUTICS

Acute Immediate Reactions to Penicillin. G. W. Lewis. Brit. M. J. 1:1153-1157 (May 18) 1957 [London].

Acute immediate reaction after injections of penicillins occurred in 12 patients from general practice. They were divided in 3 groups. The first group consisted of 2 physicians; 1 of them had a painful boil inside his nostril and was given an injection of 1 million units of crystalline penicillin followed immediately by one of 900,000 units of procaine penicillin in aqueous suspension. Nausea, swelling of the upper lip, and a greatly accelerated and irregular pulse rate developed 15 minutes after the injection and were followed by loss of consciousness for 2 hours. One week later large urticarial lesions occurred over the entire body. A similar reaction occurred in the other physician after an injection of procaine penicillin in aqueous suspension which he administered to himself. Both men had received many previous injections of penicillin, and it is suggested that the untoward reaction was due to intramuscular injection of penicillin in sensitized persons. Group 2 consisted of 6 patients, 3 men and 3 women between the ages of 34 and 60 years. Two of these patients received crystalline penicillin and 3, procaine penicillin, and the reactions in these were produced by accidental intravascular injection or back-seepage in slightly sensitized persons. The 6th patient had been given an injection of penethamate hydriodide, and his reaction may have been due to the known toxicity of this compound, since subsequent injections of procaine penicillin were given without untoward reactions. The third group consisted of 4 patients, 2 men and 2 women between the ages of 21 and 56, in whom the reactions were caused by accidental rapid intravascular injection of procaine penicillin suspensions.

A scheme for minimizing the incidence and severity of these reactions is outlined. It includes reduction of incidence of sensitization, by confining oral and parenteral administration of penicillin to cases with clear indications and by abandoning topical application of penicillin; careful history-taking; and dermal and intradermal tests with solutions of crystalline penicillin in allergic patients with previous mild reactions. The interval between individual injections of a course of penicillin should never exceed 10 days, the time required for sensitization to become established. Careful technique of injection should be used. All patients who once had an acute immediate reaction from the administration of penicillin should be given a card indicating this fact, and this card should be carried in the wallet or handbag. Suggestions are made for treatment.

BOOK REVIEWS

Human Cancer: A Manual for Students and Physicians. By Maurice M. Black, M.D., Associate Professor of Pathology and Clinical Pathology, New York Medical College, New York, and Francis D. Speer, M.D., F.C.A.P., Professor and Director, Department of Pathology and Clinical Pathology, New York Medical College. Cloth. $7.50. Pp. 273, with 34 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1957.

In this compact volume the authors have accomplished a synoptic presentation of human cancer in terms of its biological behavior correlated with clinical manifestations and indications for treatment. Although they emphasize the importance of the balance between host and tumor as the chief factor in prognosis, they do not neglect the importance of diagnosis and treatment at an early stage when possible. The book fulfills its objective well, particularly in the first five chapters which deal with cancer detection, human carcinogenesis, biological behavior of cancer, biochemistry of cancer, and chemical and radiation therapy. The remainder of the book deals briefly with cancer in anatomic sites and systems and with remarks as to incidence, signs and symptoms, structure, metastases, prognosis, and treatment. In general, these brief and up-to-date reviews of various types of cancer provide valuable information for medical students and physicians with a general interest in the treatment of cancer.

The one defect in the book is a tendency toward dogmatic statements. Examples of this are found in such recommendations as estrogenic therapy for palliation of mammary carcinoma in patients 60 years of age and older, while the generally accepted attitude is the use of antiandrogenic treatment based on physiological age or at five years or more after the menopause. The recommended intramuscular dose of testosterone propionate for palliation of mammary cancer is somewhat greater than that commonly used at present; 50 mg. three times weekly produces the same limited benefits in premenopausal women as does twice this amount. The authors state that only 32% of thyroid carcinomas are of the papillary variety but, in most series, over 50% of thyroid cancers are papillary adenocarcinomas. Hemithyroidectomy is recommended as the treatment for thyroid cancer; there is no mention of the possible advantages of total thyroidectomy. The experience of the authors in chemotherapy of mammary cancer seems to have been more favorable than that of most of the investigators, particularly with respect to triethylene thio phosphoramide, a drug that has been of little value in the experience of most qualified investigators. The volume is well supplied with tables, graphs, and occasional photomicrographs of excellent quality. There is a comprehensive index. An extensive bibliography appears at the end of each chapter.

A Manual of Pharmacology and Its Applications to Therapeutics and Toxicology. By Torald Sollmann, M.D. Eighth edition. Cloth. $20. Pp. 1535. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1957.

This new edition of a textbook, first published at the turn of the century, is written by one of the founders of American pharmacology. As one indication of the speed with which pharmacology is moving, it might be pointed out that probably over 50% of the drugs in popular use today were not known when the last edition of this book was published in 1948. The aim of this textbook "is to furnish a guide through the complexities of modern pharmacology—the actions and uses of drugs," in association with a critical summary of the chief features of the many contributions made in this ever expanding field. It is presumably prepared primarily for use by medical students. The book is well indexed and, as is to be expected with a book of this type, it is indexed in terms of drugs rather than of diseases for which the drugs are used. As in the earlier editions, only the more recent references (in this case those since 1940) are listed. Despite this limitation, about 11,000 references are included in the appendix. The pharmacology of drugs and other chemicals of possible medical and biological importance is discussed in the classical manner: origin, chemical and physical properties, absorption, fate, actions, uses, dosages, and the signs, symptoms and treatment of overdosage. Details of experimental findings are given to an extent not found in the usual textbook in pharmacology, thus providing a valuable source of information to the researcher in this field. Introductory chapters deal with certain aspects of pharmacy important to the prescriber such as prescription writing, factors influencing the intensity of drug action, and certain general fundamental concepts of the mechanism of drug action.

As is inevitable in a book of this encyclopedic nature and in this field, there are some errors and controversial statements. One of these, for instance, is the statement to the effect that during digitalis therapy in mammals the size of the heart is not diminished in diastole but only in systole. Most writers on this subject now are of the opinion that in human beings, after full therapeutic doses have been given, a decrease in diastolic size results both

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in normal subjects and in patients with congestive heart failure. Again, in the opening paragraph on digitalis, it would appear that singling out the actions of digitalis effective in overcoming decompensation in valvular cardiac lesions lays undue emphasis on digitalis usage in such conditions. It would have been preferable to cite auricular fibrillation with failure as the outstanding example, as is done later. It is further stated that pigeons tolerate 25 times as much digitalis as do cats on intravenous injection. Reference to the original work cited, however, shows that pigeons are only 25% more tolerant than cats. For the average medical student and practitioner, the ready usefulness of the book would have been improved if more clear-cut comparisons (preferably in tabular form) of drugs having a similar general type of action or use, such as the various members of the digitalis group, the anticoagulants, the antihistaminics, and the opiates had been included. Like its predecessors, this edition will be a standard reference book for students, practitioners, and research workers, not only for the purpose of keeping abreast with pharmacology generally but for the specific purpose of finding what studies have been done, and by whom, on a particular drug or chemical. It is a vast reservoir of pharmacological information.

Practical Psychiatry for Industrial Physicians. By W. Donald Ross, M.D., B.Sc., F.R.C.P., Associate Professor of Psychiatry, University of Cincinnati, Cincinnati. Foreword by Robert A. Kehoe, B.S., M.D., Professor of Industrial Medicine and Director Department of Preventive Medicine and Industrial Health, Institute of Industrial Health and Kettering Laboratory, University of Cincinnati. Preface by Maurice Levine, A.M., M.D., Professor of Psychiatry and Director of Department of Psychiatry, University of Cincinnati. Cloth. $7.50. Pp. 401, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1956.

Because of the numbers of people contacted and the amount of time spent in employment, industrial medicine possesses an ideal structure for the application of mental health procedures. An average work week is about 25% of the working person's waking time. In view of the fact that these hours are intimately related to the economic security of the country and have special dynamic meanings for the worker himself, it is to be wondered that recognition and growth of the psychiatric side of industrial medicine was so late. The present volume is one of very few to present the multifaceted psychiatric aspects of medicine in the industrial world. The author cites much material from his own experience and from that of physicians in industry at large. He discusses motivation, fatigue and boredom, morale and absenteeism, accident proneness, job stress, and various other industrial medical problems. The first two sections consist of a short orientation in basic psychiatry. Interviewing and history-taking techniques are reviewed. The author cites the 1952 American Psychiatric Association "Diagnostic and Statistical Manual" for classification, and he leans heavily on Levine's "three layer approach" for psychotherapy. Part 3 deals with the place of medicine in industry, allied social sciences, and communications and referrals.

In the 18 chapters devoted to specific problems, many important and provocative concepts are presented. These should be of interest to the psychiatrist attempting to understand his patient and to the industrial physician seeking psychiatric orientation. In-plant and out-of-plant problems may be diagnostically separable, but they are often best understood as cause and effect (in either direction). Psychodynamics and the physician's contribution are discussed in relation to each type of problem. Throughout the book the author makes many interesting generalizations. For example, he compares the value of the neurotic in industry to the canary in mining; he is unusually sensitive to the stresses that affect everyone. Thus, with perception and insight, the industrial physician can forestall more widespread trouble or discontent. Again, the author emphasizes the need for the physician to be a medical advisor to management and to avoid personnel policy matters if he is to be of real value. The physician must be free to learn of the informal organization of his industry via rapport with lower echelons, and he must have access to the top in order to facilitate his communications which require executive action. This volume should be of value to industrial physicians. It should also provide good orientation for psychiatrists who accept referrals from these physicians.

Practical Refraction. By Bernard C. Gettes, M.D., Assistant Professor of Ophthalmology, Graduate School of Medicine, University of Pennsylvania, Philadelphia. Cloth. $6.50. Pp. 170, with 58 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1957.

This book represents an attempt to produce a short manual on the technique of refraction without going into the details of physiological optics on which refraction is based. For that reason the neophyte will not find that this book is adequate for all his needs but should find in it many useful suggestions. While most of the book is clearly written and should be intelligible to the beginning student in refraction, certain parts, such as the description of astigmatism, are likely to be confusing. Most writers on refraction are extremely dogmatic as to the correctness of their own methods and the error implicit in all other methods, but this author is to be congratulated on his broad viewpoint and the recognition that all techniques have their advantages but that experience, skill, and accuracy are the most essential factors. The orthodox method of presentation has not been fol-

lowed in this text, but the subject matter is taken up in the following order: preliminaries to sight testing, astigmatism, accommodation, cycloplegia, subjective methods of testing, hyperopia, refraction of the aphakic eye, myopia, presbyopia, ophthalmic lenses, contact lenses, and aids for subnormal vision. Whether this is a more logical sequence of presentation may be open to question, but this is probably not a matter of great moment. If the student of refraction has several textbooks, he should find this a useful addition to his library.

Developmental Abnormalities of the Eye. By Ida Mann, C.B.E., M.A., D.Sc. With foreword by Sir John Herbert Parsons, C.B.E., D.Sc., LL.D., and introduction by Conrad Berens, M.D., F.A.C.S. Second edition. Cloth. $15. Pp. 419, with 284 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; 2083 Guy St., Montreal, Canada, 1957.

Because of her wide and extensive knowledge of heredity, embryology, and genetics, the author has ably segregated anomalies, abnormalities, and developmental arrests. She has also explained their probable causes. The ophthalmologist is made aware of the importance of the proper psychological approach to the parents of a child with an ocular abnormality. He also will be impressed with the urgent need for early corrective surgery in a child with a coloboma of the eyelid, buphthalmos, or complete congenital cataracts in order to spare the child and its parents real psychic trauma. Psychologists and psychiatrists should also profit from reading this book.

Morphine & Allied Drugs. By A. K. Reynolds, Ph.D., and Lowell O. Randall, Ph.D. Cloth. $10. Pp. 393, with illustrations. University of Toronto Press, Toronto 5, Canada; Oxford University Press, Amen House Warwick Sq., London, E.C.4, England, 1957.

This monograph presents a wealth of information on the potent analgesic drugs in a single volume. In view of the mass of literature on morphine and the morphine-like drugs, the task of preparing a comprehensive treatise on this subject was formidable. The authors have accomplished this objective in a capable manner. While not intended to be a complete review of the literature, this book does provide extensive information on the pharmacology of most of the known papaveraceous alkaloids and related synthetic substances. Morphine, the oldest, most widely used, and the most studied of all the alkaloids of opium, is discussed in the greatest detail. In addition to its pharmacology and toxicology, the chemistry, absorption, fate, and metabolism of morphine have received considerable attention as well as many aspects of the addiction phenomenon. Its therapeutic uses are briefly mentioned. The other natural and semisynthetic alkaloids, including those bases found in species other than Papaver somniferum, are also discussed in detail. Many alkaloids related to morphine, which are primarily of historical and academic interest, have been included for the sake of completeness. The chemistry and pharmacology of the newer and more important synthetic analgesics, including meperidine, methadone, alphaprodine, and certain of the morphinan compounds, have been adequately covered. The final sections of this volume are devoted to the analgesic antagonists and to theories of analgesia based on structural-activity relationships. There is a subject index as well as an extensive bibliography. Typography and binding are excellent.

Research on newer analgesics continues at a rapid pace in an effort to develop compounds with the potency of morphine and its congeners but without the addicting liability and other undesirable effects of the opiates. Although the ideal analgesic has not, as yet, been found, recent developments have already provided several synthetic substances with sufficient potency to eliminate the former exclusive dependence on morphine and its constituents for the relief of pain. This timely and well-presented review should therefore be welcomed by pharmacologists and synthetic chemists in this rapidly advancing field.

The Rehabilitation of Speech: A Textbook of Diagnostic and Corrective Procedures Based upon a Critical Study of Speech Disorders. By Robert West, Professor of Speech and Director of Speech and Hearing Center, Brooklyn College, Brooklyn, Merle Ansberry, Professor of Speech and Director of Speech and Hearing Clinic, University of Hawaii, Honolulu, and Anna Carr. [Book One: The Pathology of Speech and the Rationale of Its Rehabilitation. Book Two: Remedial Principles.] Third edition. Cloth. $7.50. Pp. 688, with 59 illustrations. Harper & Brothers, 49 E. 33rd St., New York 16, 1957.

This third edition of a book first published 20 years ago reflects growing interest in speech therapy on the part of physicians, psychologists, teachers, students, and nurses. Designed in the beginning for clinicians and professional workers engaged in speech rehabilitation, it provides much helpful data and material, copious comments on the rationale of rehabilitation, and numerous bibliographic suggestions. The latest edition of this work maintains the sound standards of its predecessors and is a welcome addition to basic sources of information dealing with the rehabilitation of speech.

Essentials of Clinical Proctology. By Manuel G. Spiesman, M.D., B.S., F.I.C.P., Associate Professor of Proctology, Chicago Medical School, Chicago, and Louis Malow, M.D., B.S., F.A.C.S., Associate in Surgery, Chicago Medical School. Third edition. Cloth. $8.75. Pp. 316, with 130 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W.C.1, England, 1957.

Students and general practitioners should find this volume a store of practical information. The book is based on the teachings and practice of the authors and is well illustrated. The more curious reader will find here the English concept of "pectenosis" based on chronic passive congestion. He will wonder, no doubt, what causes the chronic passive congestion. The book would have been better if more attention had been given to diverticulosis and to diverticulitis.

QUERIES AND MINOR NOTES

WHEAT GERM, UNSATURATED FATTY ACIDS, AND ATHEROSCLEROSIS

To the Editor:—*It is claimed that the oil of wheat germ contains unsaturated fatty acids, particularly linoleic acid, in addition to sitosterol, both of which are said to be of benefit in preventing arteriosclerosis. Can these facts be considered true?* M.D., *Florida.*

Answer.—Depending on the variety from which it is obtained, wheat germ oil contains anywhere from 30 to 57% (weight) linoleic acid (Hilditch: Chemical Constitution of Natural Fats, ed. 3, New York, John Wiley & Sons, Inc., 1956). In addition, wheat germ probably contains small amounts of plant sterols in the form of sitosterol. Some of the other known components include naturally occurring vitamins, choline, inositol, *p*-aminobenzoic acid, and traces of many minerals.

Unsaturated fatty acids have been shown to reduce blood cholesterol levels, as measured in the laboratory, but it must be emphasized that to date no definite relationship has been proved that lowering of blood cholesterol by administration of unsaturated fatty acids specifically prevents atherosclerosis or subsequent coronary diseases.

TREATMENT OF ALLERGIC REACTIONS TO PROCAINE

To the Editor:—*What is the best treatment for a mild, a moderate, and a severe allergic reaction after the use of procaine (Novocaine) hydrochloride or its derivatives?*

Robert F. Brennen, M.D., Fullerton, Pa.

Answer.—One may assume that the allergic reactions referred to are not the usual contact types of dermatitis that are relatively common from the use of procaine or its derivatives. The anaphylactic types of reaction (respiratory, urticarial, vascular, and possibly other visceral types) after the administration of procaine are infrequent.

The danger from an anaphylactic type of reaction after the administration of any antigen (drug or protein) is usually proportional to the rapidity of the onset of the symptoms. The earlier the symptoms follow the administration of procaine, the sooner countermeasures should be taken, without loss of precious time for evaluating the severity of the symptoms. Allergic symptoms that occur within seconds after the administration of the drug (itching, either generalized or of the palms, soles, or scalp; respiratory symptoms such as sneezing; dyspnea with or without wheezing; or evidence of circulatory collapse not due to syncope) are dangerous and must be treated without loss of seconds. The sooner epinephrine 1:1,000 is administered, the better the chances of recovery. One-half milliliter of this solution should be administered subcutaneously. If necessary, the dose may be repeated in five minutes and again in another five minutes.

The danger from an overdose of epinephrine is less than from the progression of an immediate anaphylactic reaction. Symptoms of an excessive dose of epinephrine (throbbing headache, rise in blood pressure, or cardiac arrhythmia) can be controlled by application of a tourniquet above its injection site and by releasing this tourniquet for brief periods every 10 to 20 minutes until the symptoms are tolerable. If the procaine has been injected subcutaneously rather than intravenously, at a site that can be isolated from the general circulation by a tourniquet, this should be done without delay. If circulatory collapse occurs (to be quickly and carefully differentiated from syncope), epinephrine may have to be given intravenously (0.1 to 0.2 ml. of 1:1,000 solution, diluted quickly with a few milliliters of saline solution or the patient's own blood and injected slowly over a period of one or two minutes). This is a dangerous procedure in patients with myocardial insufficiency. Intravenous administration of plasma with or without norepinephrine solution may be necessary in patients with prolonged circulatory collapse and hypotension.

Other measures have been recommended for severe anaphylactic reactions. It is this consultant's opinion, from personal experience, that one should rely primarily on the adequate and early use of epinephrine and in selected cases on 7½ grains (0.5 Gm.) of aminophylline administered intravenously, rather than diffuse one's efforts on less effective measures. Moderate or mild anaphylactic types of reaction, either subsequent to a severe reaction or as primary occurrences, may be controlled by antihistamines, by ephedrine preparations, or by corticotropin (ACTH) or corticoids. The last-mentioned are useful in prolonged reactions, since the condition is self-limited. Neither corticotropin, nor corticoids, nor antihistamines should be solely relied on for controlling a rapidly occurring, explosive anaphylactic type of reaction. Hormones act too slowly to meet the emergency, and antihistamines, even administered intravenously, are inadequate for overcoming a severe anaphylactic reaction.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

PREMATURE ERUPTION OF TEETH

To the Editor:—*A dentist states that a 6½-year-old boy has "teeth that are coming in five years ahead of time" and that these teeth "have so many cavities that he will have no teeth left by the time he reaches adulthood." His deciduous teeth also showed many cavities, and many of them had to be extracted. The dentist feels that this indicates some systemic disease. Complete physical examination reveals a boy who is tall for his age and in excellent physical and mental health. There are no congenital abnormalities apparent nor any evidence of disease. Serum calcium, phosphorus, and alkaline phosphatase levels are within normal limits for his age. A careful nutritional and hygienic history indicates that the child eats well of all foods, including those containing calcium and proteins, meat as well as milk, and brushes his teeth frequently. He does not overindulge in bottled sodas, orange juice, or milk to the extent of spoiling his appetite for meat. His ancestry is mixed Irish, German, and English, so that, for the present, his Irish ancestors are being blamed for his dental difficulties. Please suggest further investigation, possible diagnosis, therapy, and prevention. If each decalcified area is filled as early as possible, is there any reason why the child should lose his permanent teeth any earlier than anyone else?* *Shepard G. Aronson, M.D., New York.*

This inquiry has been referred to three consultants, whose respective replies follow.—Ed.

Answer.—Premature eruption of teeth may occur in hypergonadism, which may be secondary to hyperpituitary function or, more rarely, hyperthyroidism. The degree of premature tooth eruption cannot be evaluated, since this information is not available. Blood chemistry findings would not be altered in rampant caries. The diet should be well balanced and low in fermentable carbohydrates.

The patient's dentist should seek the services of a caries control laboratory. The relative susceptibility of this patient to caries and the effectiveness of the caries control procedures can be evaluated by means of counts of lactobacilli. With frequent expert dental care and complete patient cooperation, there is no reason why the permanent teeth should be lost prematurely. Dental caries are related primarily to local environment factors that can be controlled.

Answer.—To begin with, it must be borne in mind that there is extensive variation in the eruption pattern of both deciduous and permanent teeth and that the statement that the teeth "are coming in five years ahead of time" in itself is almost impossible to interpret. The lack of any evidence of a systemic disease would strongly suggest that this child's problem is entirely local. There is every reason to believe that if the extensive caries are managed on the basis of individual cavities the child should be able to maintain many of his teeth well into adult life. The question as to whether or not each decalcified area should be filled as early as possible to avoid the loss of more permanent teeth is the essence of the problem. Certainly this procedure should be followed, and the results should be acceptable. It is recommended that good local dental care be given the child in order to prevent the spread of the carious lesions and to maintain the teeth which are now forming the dentition.

Answer.—Tooth eruption normally occurs over a wide age range around the accepted average. Hyperthyroidism and hyperpituitary disease are associated with accelerated tooth eruption. Caries resulting from systemic disease most often result from defective formation of enamel predisposing to bacterial erosion of the teeth. From the description this child has no significant systemic disease. The early loss of teeth will often result in minor degrees of malocclusion, which predisposes to food being trapped and permitting overgrowth of oral bacteria with enamel erosion and caries formation. The age-periods 5 to 8 years and 12 to 18 years are periods of an unusually high incidence of caries. The best management in such a case is good oral hygiene and early filling of cavities with close supervision by the dentist. If teeth become so badly diseased that they must be extracted, space retainers should be used to maintain proper occlusion. No accurate prognosis can be given, but with proper care the child should have functioning teeth for quite a while.

STEROIDS AND PERITONITIS

To the Editor:—*Please comment on the use of cortisone and other steroids in the management of severe peritonitis, such as occurs in cases of ruptured appendix.*

William R. Moses, M.D., Washington, D. C.

Answer.—The true value of corticosteroids and corticotropia in the therapy of peritonitis is unknown. Attention has been called to the benefits of the so-called anti-inflammatory and toxin-blocking effects of these hormones, but knowledge of the mechanisms and significance of these phenomena is incomplete. These agents have also been shown to inhibit antibody formation in some situations, and it is clear that clinical evidence of an infection's progression or even an intra-abdominal catastrophe may be obscured by steroid therapy. Thus, the question of their use is controversial.

In spite of this contradictory evidence, however, it is certain that relative adrenal insufficiency at times accompanies overwhelming sepsis. To this extent a dogmatic statement condemning the use of steroids for peritonitis is unacceptable, and the following policy seems justified and practical at the present time. The patient suspected of having relative adrenal insufficiency secondary to previous steroid therapy deserves hormone treatment in a stressful situation, such as peritonitis, particularly if surgery is contemplated. Exclusive of this group, there are patients with peritonitis

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who do not respond to preparation for definitive surgery by the intelligent use of accepted supportive measures. The addition of steroid therapy in the management of such patients is probably justified. It must be emphasized, however, that these agents are not substitutes for conventional measures. Strict attention must be paid to the surgical, antibiotic, fluid, and electrolyte needs of the patient. The plasma deficit resulting from the peritoneal "burn" must be appreciated and replaced. It is likely that this aspect of treatment is often neglected.

The surgeon responsible for the care of the patient receiving steroids must not be misled by the clinical improvement which may attend such therapy. This apparent improvement should not influence a previously formed opinion regarding the indication and need for surgery. Steroid therapy, once started, should be continued throughout the course of an acute illness. Withdrawal of these agents should be gradual and cautious, and it is suggested that hormonal treatment be terminated before antibiotics are withdrawn. In summary, these agents are not substitutes for either clinical judgment or proper surgical and supportive therapy. Used intelligently and cautiously, they may at times be helpful in the preoperative preparation or the postoperative management of patients with severe peritonitis.

ISOLATION OF PARAKEETS TO PREVENT TRANSMISSION OF PSITTACOSIS

To the Editor:—*In Queries and Minor Notes in the March 9, 1957, issue of* The Journal, *page 909, under the heading of "Hazard of Parakeets in Hospitals," most pertinent questions in regard to hazards from these birds seemed to be answered except one which seems to be of considerable practical interest. Presumably, the usual custom is to purchase one bird which is then isolated in a cage, entirely away from other birds, in the home, hospital, or elsewhere. How long a period of isolation is necessary so that the bird will be presumed to be unable to transmit psittacosis if it remains healthy?*

Maurice A. Walker, M.D., Kansas City, Kan.

Answer.—Incipient psittacosis cannot be detected in psittacine birds except by virus isolation, which requires killing the bird. Apparently healthy parakeets may spread the virus throughout their lives. Latency is essential to the psittacosis parasite to maintain its infection chain. From 5 to 20% of immature parakeets offered for sale may be infected. The majority of these young birds free their tissues of this infectious agent within a few months, but some never lose the virus. During their "convalescence" they may be, or may become, shedders when subjected to certain stresses—adaptation to a different environment, excessive fondling, chilling, and such factors.

The following experiment vividly illustrates that it is impossible to set a definite time at which a parakeet can be declared not contagious. A parakeet fatally infected four older persons before its death from psittacosis; its cagemate appeared healthy. For six months thereafter, when this cagemate was kept in a closed glass cage in the laboratory with a succession of highly susceptible ricebirds introduced at intervals as cagemates, these ricebirds died of psittacosis. After that time ricebirds introduced did not become infected, but 10 months after the latently infected parakeet had been picked up from the household, live virus was found at autopsy in its spleen and liver.

All parakeets offered for sale should be treated for an adequate time with feed containing an adequately high concentration of tetracycline compounds. Tests in aviaries and pet shops have shown that interrupted oral treatment for 15 days with a total of not less than 30 mg. of any tetracycline compound will render the birds noninfectious, and within a month after the termination of treatment the tissues of 95 to 100% of the parakeets will have been freed from the viral agent. Certainly from the standpoint of public health, untreated parakeets should not be allowed in hospitals or households.

MILK CONSUMPTION BY ADULTS

To the Editor:—*A young man, aged 21 years, in good health, has never abandoned drinking milk with his meals. He dislikes coffee or tea and consumes at least one quart of milk daily. Should interdiction be suggested to prevent possible metabolic disturbances or the deposition of renal calculi as he grows older?*

Joseph Backlar, M.D., Richmond Heights, Mo.

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—Milk is an important source of nutrients which are needed throughout life, and its continued consumption by adults is desirable accordingly. There is no evidence justifying the interdiction of the drinking of one quart a day by a healthy adult on the basis that this use might cause metabolic disturbance or the deposition of renal calculi.

Answer.—The question pertaining to "potential metabolic disturbances" suggests cholesterol metabolism. This whole subject is still in the realm of active research. If fat intake seems most important in this connection, one should recognize that milk is by no means a high-fat food (when it contains 3.9% fat by weight, giving 51.3% of the total calories). On this basis milk would not seem to be the first food to be eliminated to reduce fat intake. If atherosclerosis were known to exist or if blood cholesterol levels were unusually high, the use of milk reduced in fat might be considered. This choice, however, may be contraindicated when one considers the question pertaining to kidney stones. Some evidence has been reported relating renal calculi to vitamin A deficiency in animals. If there were any question of diabetes or other

metabolic disturbance interfering with the formation of vitamin A from carotene, the 1,600 I. U. or more of preformed vitamin A obtained from a quart of whole milk would be a safeguard. So far as the possibility that the one quart plus other intake of milk would make calcium intakes so high as to raise question of supercalcification is concerned, apparently even doubling the normal level of calcium intake has no such effect in the normal individual. Again, only if the patient already had evidence of renal calculi or belonged to a family where the incidence of stones is high would there seem to be any reason to anticipate problems related to the levels of calcium intake which are suggested by the ingestion of even more than one quart of milk daily. Until further evidence is available, it would seem reasonable to permit this normal young man to continue to enjoy his quart or more of milk per day.

RESIDUAL IODIZED OIL IN THE BACK

To the Editor:—*A patient has complained of vague low back pains, essentially in the lumbar and sacroiliac areas, for the past year; for the past four weeks he has complained of areas of neuralgic pain over the skin of the right lower quadrant and at times the right thigh and right knee. The pain in the right thigh and right knee does not seem to follow the course of sciatic radiation. It is fleeting in character but may persist for hours; it is relieved to considerable extent by analgesics. Fifteen months ago a large intervertebral ruptured disk was removed between L-4 and L-5 to relieve severe root pain in the left ankle and the lateral aspect of the left foot. The disk was sequestrated, and after this surgery the root pain and numbness in the left foot were relieved. Yet, the vague lumbar aches and neuralgic pains over the right lower quadrant, right knee, and right thigh, anteromedian, persist. Recent x-rays reveal that "numerous small and large opaque droplets, presumably representing Pantopaque or Lipiodol, are present in the lower lumbar subarachnoid space; there is a suggestion of an operative defect in the region of the articular processes of L-4 and L-5 on the left side." Spinal fusion was not done as instability did not seem to be too marked. Could the residual iodized oil be responsible for the neuralgic picture and the vague low back pains? Should another attempt be made to remove these radiopaque mediums, even though the operator attempted to do so at the time of making the myelogram but was not successful?*

M.D., Florida.

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—It is not believed that residual iodized oil is responsible for the vague aches and pains of which this patient complains. If the oil is broken up into small droplets, it would be impossible to remove it, even though the cauda equina were exposed surgically. Suggestions include rest, support, mild analgesics, heat, and any other conservative therapeutic measures, including encouragement, which are available. If symptoms become worse, further extrusion of disk material on the other side or at a higher level should be considered as a possible cause of complaints.

Answer.—The question of whether residual iodized oil within the subarachnoid space causes irritation and symptoms has been debated pro and con for years and probably dates back to the first use of this substance. The literature contains a number of articles supporting the contention that it does cause symptoms. The fact that there is a paucity of statistics to support the other side of the argument is of no moment. Patients who do not have symptoms do not present themselves for study. There must be many thousands of patients going about their normal daily activities in the United States with varying amounts of these nonabsorbable oily substances within the subarachnoid space. It is rarely possible to remove every droplet of this oil after making a myelogram. Most of the patients who have this oil within the spinal canal do not realize that it is there. Extensive review of the literature has not been carried out, but this consultant is not aware of any series of cases in which the removal of residual oil as a sole treatment for symptoms arising in the spinal canal and attributed to arachnoiditis has resulted in relief of symptoms.

If it can be determined by means of gravitational flow that the residual iodized oil in this patient is mobile, there would seem to be no harm in attempting its removal. However, previous to its removal it is suggested that some oil be added and that myelography be repeated. A recent series of myelograms done immediately after the removal of herniated disks have indicated that the defects seen in the preoperative myelograms persist postoperatively in some cases. This work is not yet published. It is this consultant's opinion that, if it can be determined that the residual symptoms are arising from the fourth interval, fusion of this interval of the distraction type should be carried out

ALCOHOL AND GLYCERYL TRINITRATE FOR MYOCARDIAL INFARCTION

To the Editor:—*Please comment on the alleged danger in the use of glyceryl trinitrate (nitroglycerin) and/or alcohol in a coronary attack.*

M.D., California.

Answer.—The expression, "in a coronary attack," is interpreted to mean the pain associated with acute myocardial infarction. As a rule, this attack of pain is severe, and the use of morphine is indicated to control the pain. The use of glyceryl trinitrate is indicated in attacks of pain caused by angina pectoris brought on by effort. Patients who have myocardial infarction often are in shock, and their blood pressure is low. Glyceryl trinitrate tends to lower the blood pressure. It usually is considered to be contraindicated, because of this factor, when myocardial infarction is present.

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Alcohol has no specific action which modifies the damage after acute coronary arterial insufficiency. Moreover, by the vasodilating action of alcohol, blood pressure is lowered and the insufficiency of the coronary circulation is further increased. Hence, on scientific grounds, there is no indication for the use of alcohol in the presence of myocardial infarction.

RE-TREATMENT OF SYPHILIS

To the Editor:—*In 1942 a 42-year-old man had a history of a penile sore at the age of 22. Serologic examinations revealed 4+ Wassermann and Kolmer reactions, a clear spinal fluid with a cell count of 60 per cubic centimeter, a 4+ spinal fluid reaction, and a paretic type of colloidal gold curve. Between May and August of 1942 the patient was given a total of 39 Gm. of tryparsamide. Subsequent tests in 1946 included a spinal tap, with all tests negative, no colloidal gold curve, 2+ Wassermann and Mazzini reactions, a doubtfully positive Kolmer reaction, and a doubtful 1+ Kahn reaction. In May, 1947, the Wassermann and Mazzini reactions were 4+; the Kolmer reaction was 2+. In August, 1947, the Mazzini reaction was 4+, and the Kolmer reaction was 4+. In 1954 the patient came in complaining of dizziness. Further tests showed a doubtful 2+ Mazzini reaction and a weakly reactive Venereal Disease Research Laboratory test. The patient was referred to a neurologist who felt that he should have a repeat spinal tap and that his then present condition was a manifestation of syphilis of the central nervous system. The patient, however, refused to have another spinal tap because of a severe headache after his last one. This year the patient came in for an insurance examination. Blood serologic tests revealed a weakly reactive Venereal Disease Research Laboratory test and a nonreactive Kolmer test. A spinal tap revealed a clear fluid with a total protein content of 32 mg. per 100 cc. Venereal Disease Research Laboratory and Kolmer tests were both nonreactive. At the suggestion of the state laboratory a Treponema pallidum immobilization test was done on March 30, 1957, and was reported by the Communicable Disease Center, Venereal Disease Research Laboratory, Chamblee, Ga., as follows: Treponema immobilization test, reactive; Treponema immobilization complement-fixation test, reactive. The only positive sign of syphilis is a slightly larger right pupil, but both pupils react to light and accommodation. The patient is completely asymptomatic and apparently has had no treatment since the original treatment with tryparsamide in 1942. How should he be treated?*

E. G. Bourns, M.D., Westfield, N. J.

Answer.—The patient in question should now be treated with 6 to 10 million units of a repository penicillin product, e. g., procaine penicillin-in-oil or Bicillin, given in 10 to 16 injections two or three times a week. This advice is given not because of the persistent blood serologic tests or of the positive Treponema immobilization and Treponema immobilization complement-fixation tests in blood and/or spinal fluid; these are of relatively little importance. It is also given in spite of the fact that the most recent examinations of the spinal fluid (cell count not stated) are normal as to total protein content and serologic tests.

The advice is given because the inquirer indicates that the only antisyphilitic treatment which the patient has had for neurosyphilis (presumably asymptomatic in 1942) was 39 Gm. of tryparsamide. This is not enough treatment to provide him with much security for the future. The penicillin treatment advised may be regarded as prophylactic and should offer him about 95% security for the future.

DRYNESS OF MOUTH AND TONGUE

To the Editor:—*A patient, aged 70 years, has had an absolute dryness of the mouth and tongue for the last two years. Examination is negative except for moderate obesity and associated hypertension, which has been corrected, and mild conjunctivitis. The salivary glands are not unusual. Complete blood cell count, urinalysis, nonprotein nitrogen level, blood cholesterol level, and blood electrolyte concentrations are all within normal limits. Basal metabolic rate and radioiodine (I^{131}) uptake are normal. The patient is not a mouth breather. He states, however, that there are occasional periods in which the mucous membrane has a little moisture. What can be done to help this patient?*

J. Will Fleming Jr., M.D., Moberly, Mo.

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—It is possible, and perhaps likely, that the medication used for control of hypertension is responsible for the dryness of the mouth and tongue. This is a common complaint of patients who are receiving Rauwolfia-like preparations. Dry mucous membrane in the mouth is sometimes seen in association with the pharyngitis sicca which usually accompanies both true atrophic rhinitis and the atrophic type of chronic rhinitis often present in elderly people. The latter may evidence endocrine changes after the male or female climacteric. Checking hypertensive drugs used for this patient and the administration of potassium iodide, 0.3 Gm. three or four times daily, together with an adequate fluid intake, might help this patient.

Answer.—The condition described would seem to meet the requirements for classification as Sjögren's syndrome. According to Dorland, this syndrome is characterized by "dryness of all mucous membranes, resulting from deficient secretion of the glands, particularly the lacrimal and salivary glands, those of the upper respiratory tract, the sweat glands, and the glands of the stomach." The syndrome usually appears in elderly people. There is no known treatment which has a general effect. Locally, artificial tears can be

used in the eye whenever the symptoms require. The most satisfactory of the artificial tears is Isopto-Alkaline Ophthalmic Solution. Cortisone applied locally to the eye has an ameliorating effect for some patients who have this syndrome, but when it is taken by mouth it is of no value.

STERILIZATION OF SHOES

To the Editor:—*Is there a method of sterilization of rental shoes with skates which the owner of a roller-skating rink might use to cut down the incidence of "athlete's foot"?* *M.D., Pennsylvania.*

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—There is no satisfactory method of sterilization of shoes. Strong fungicides, such as formaldehyde, even if effective would cause in some individuals an irritation and sensitization. Furthermore, they would in time damage the shoes. It is therefore recommended that to keep the feet and shoes dry a bland dusting powder composed of the following be used: bismuth subgallate, 1½ dr. (5.8 Gm.); zinc sterate, 3 dr. (11.6 Gm.); amylum, 4 dr. (15.5 Gm.); and talcum, 4 oz. (124.4 Gm.). This powder should be sprinkled in the shoes before and after they are used.

Answer.—In "Diseases of the Skin" by Ormsby and Montgomery (ed. 8, Philadelphia, Lea & Febiger, 1954), there is the following passage on sterilization of shoes:

> Cleanse the shoes of extraneous debris with mild soap and water; dry with a cloth; place a wad of cotton in each shoe and spread out to form an insole; pour onto this insole (in each shoe) 1 teaspoonful of solution of formaldehyde (U.S.P.) diluted in 1:10; put shoes in paper box; close and wrap in paper and leave shoes in box at least six hours; remove shoes from box, remove and discard cotton; place them in air for twenty-four hours; apply saddle soap to all parts of shoes, and allow to dry; polish. The formaldehyde can be neutralized by placing the shoes in a 0.5 per cent solution of sodium bisulphite for two minutes.

For a business organization, carrying out the above would be a very difficult assignment. Finding competent, conscientious help would be an insurmountable difficulty. There is also to be taken into consideration the effect of formaldehyde on leather, and the use of aqueous solutions on leather would be harmful as well as dangerous owing to the use of metal and leather. It would probably be better to impregnate socks in a fungistatic or fungicidal solution, dry same, and supply each customer with same, compelling use over the customer's own socks. The best idea would be to compel each person to supply his own shoes with skates. At the present time, when parental monetary allowances have assumed such fantastic proportions or odd jobs offer such rich monetary rewards, this would not be a prohibitive expense especially when a contagious disease so difficult to cure is involved.

ANTICOAGULANT THERAPY

To the Editor:—*A patient was admitted to the hospital with a questionable diagnosis of a brain tumor. An angiogram was done and then a ventriculogram, after which a diagnosis of a vascular thrombosis (middle cerebral) was made. Administration of Dicumarol was ordered, with daily prothrombin time tests. The patient has been receiving this drug for two weeks prior to writing. He is about to be discharged from the hospital, and he and his family have been told by consultants that he will be all right. He is to continue the Dicumarol therapy at home, with a biweekly prothrombin time test, under his physician's supervision. The literature states that Dicumarol is a dangerous drug and that it has no effect on an already formed thrombus, its effect being simply to prevent the formation of further clots. Can the drug be given for an indefinite period of time?* *M.D., Rhode Island.*

Answer.—Dicumarol may be given indefinitely, provided that fairly frequent prothrombin determinations are made. The patient must have had his Dicumarol medication well established during his hospital stay, and therefore a continuation of the present dosage, with twice-weekly prothrombin determinations, would be quite safe. Dicumarol is a dangerous drug unless properly supervised.

The original damage from the cerebral thrombosis is still there. The purpose of the Dicumarol therapy is to minimize the dangers of repeated recurrences of clotting. It is presumed that blood cholesterol determinations have been made, for in many cases of cerebral thrombosis these levels are apt to be elevated. If such is the case, the patient should have a relatively low fat intake, in addition to his medication with Dicumarol. Both of these methods of treatment are precautionary only and do not correct the original damage.

NYLON SUTURE MATERIAL

To the Editor:—*Ordinary monofilament nylon fishing line has been used as a suture material for years with excellent results. It is now desired to use nylon skin sutures (not buried) and to sterilize this material in suitable lengths from bulk spools. Initial experiments have indicated no change in length or breaking strength after routine steam autoclaving. The material most available is ordinary fishing line of the type intended primarily for spinning reels. Is this material likely to have been treated with any chemical which might cause unfavorable tissue reaction or interfere in some other way with its use as a suture material? Also, what would be the recommended method of sterilization if autoclaving is deemed undesirable?*

Wayne E. Armstrong, M.D., Gwinn, Mich.

Answer.—While one can use ordinary monofilament nylon fishing line as suture material for skin closures, it is much preferred that nylon sutures prepared by

a reputable manufacturer of suture materials be utilized. The manufacturers of fishing lines may subject the nylon to treatment with various chemicals for the purpose of plasticizing and waterproofing the lines. Dyestuffs of unknown origin may be utilized to color the nylon fishing lines. Such treatments may vary from manufacturer to manufacturer. Suture manufacturers who label their nylon sutures as "U. S. P." products are required to meet the specifications for nonabsorbable surgical sutures as outlined in the Pharmacopeia of the United States U. S. P. XV. If a coal-tar derivative dyestuff is utilized to color a nonabsorbable suture, the manufacturer of that suture is required to utilize a dyestuff that is certified by the United States Food and Drug Administration. Nylon can be sterilized satisfactorily by autoclaving under standard conditions.

TREATMENT FOR LEPTOSPIRAL DISEASES

To the Editor:—*What is the current treatment for leptospirosis icterohaemorrhagica (Weil's disease) and leptospirosis canicola (Stuttgart's disease)? Are the spirochetes sensitive to any known antibiotic, and, if so, what is the recommended dosage?*

M.D., Montana.

Answer.—There is no really satisfactory treatment for these two diseases. Penicillin, Aureomycin, Terramycin, and streptomycin are all moderately effective in vitro, but in vivo their effect is not clear-cut. It is probable that these antibiotics are reasonably effective if given before the onset of symptoms or during the first few days of illness. Terramycin and streptomycin are probably the best. The former should be given in doses of 2 to 3 Gm. and the latter in doses of 2 Gm. a day. Treatment after the infection has become established is of doubtful, if any, benefit.

ECTOPIC GASTRIC MUCOSA

To the Editor:—*Please supply information concerning ectopic gastric mucosa. Could this be the cause of a tumor, and what is its clinical significance?*

William G. Abel, M.D., East Hampton, N. Y.

Answer.—The presence of epithelial elements of the gastrointestinal tract within the wall of the stomach is not rare. These are developmental anomalies and not true neoplasms in the sense of being uncontrolled new growths of tissue. Nevertheless, because of their gross appearance they are frequently included in classifications of benign tumors of the stomach. Terms applied to these lesions include "heterotopic or ectopic pancreatic tissue," "adenomatous tumors," and "adenomyomas." The foci of ectopic tissue, which are usually solitary, occur anywhere in the stomach and are most common in the submucosa of the pyloric portion. Grossly, these lesions may result in projecting masses or diffuse thickening of the gastric wall. Some are cystic, and occasionally a duct opening into the lumen of the stomach may be present and even demonstrated by x-ray examination. The overlying gastric mucosa, which is usually intact, may occasionally be ulcerated. Microscopically, pancreatic tissue, the duodenal glands known as Brunner's glands, and glands like those of the stomach or colon may be present. Pancreatic tissue, with acini and ducts and without islets of Langerhans, is most frequent. When the ectopic tissue is in the muscularis, proliferation of muscle about the epithelial elements, as in adenomyomas (endometriosis) of the uterus, is common. Clinical manifestations include epigastric pain, pyloric obstruction, and occasionally hemorrhage. A few reported cases of carcinoma have been thought to originate in such heterotopic tissue.

OCCUPATIONAL DISEASE IN THE TANNING INDUSTRY

To the Editor:—*Kindly supply information regarding morbidity in tannery workers who are exposed to potent chemicals.*

T. J. Kern, M.D., Hartford, Wis.

Answer.—Up to a few decades ago, the tanning industries were a prolific source of occupational diseases as to both number and variety. In 1925, Minster published a paper on hazards in the tanning industry (*J. Indust. Hyg.* **7**:299, 1925). These hazards involved both bacterial and chemical exposures. At that time the outstanding opportunities for damage centered about the chromates, benzene, hydrogen sulfide from the decomposition of organic matters, and divers tannins, both natural and synthetic, the former embracing several exotic woods, such as quebracho. There are several forms of tanning which are almost distinct enterprises. These include the tanning of sole leather, shoe leather, upholstery leather (the latter two forms involving coating operations), and, finally, special and fine skin leathers, such as those used for gloves. Synthetic leathers and substitutes for leather have enormously modified tannery operations. At the present time the exposures in the tannery industries have so well been brought under control that the incidence of occupational disease is low. The total number of diseases scarcely warrants group compilation or statistical analysis. Dermatitis remains the chief threat, with the chromates and tannins constituting the major offenders.

PSORIASIS AND GARLIC

To the Editor:—*Is there any clinical evidence that garlic extract is of any value in the treatment of psoriasis when applied topically?* *M.D., Maine.*

Answer.—Psoriasis is a therapeutically erratic disorder for which practically everything has been recommended for treatment. Garlic has been suggested for the treatment of a long list of entities. It was inevitable that the two should meet in the treatment of psoriasis. Garlic itself is not only unpleasant to the olfactory organ but is irritating to the skin when ap-

plied locally. Personal experience with the topical application of garlic has been confined to a group of lepers isolated in a separate cottage. Ambulatory psoriatics would not be pleased with the cutaneous burns produced by such applications or by the social ostracism that would greet one with garlic on the skin. Garlic extract tablets, such as those used in the treatment of hypertension, and extracts of this plant (Allium sativum) are characterized by the odor that has become diagnostic of garlic in the vicinity. Before accepting this agent as an effective treatment for psoriasis, a great deal of work is necessary to establish its efficacy in this spontaneously remittent disease, to mask its odor, and to eliminate those factors that burn the skin.

TREATMENT AFTER RADICAL MASTECTOMY

To the Editor:—*A 50-year-old woman, four years past the menopause, noted a lump in the right breast. Examination disclosed a mass about 4 in. in diameter. A frozen section showed it to be malignant, and a radical resection was performed. Pathological report showed 14 axillary nodes to be invaded by metastases. The tumor was adenocarcinoma. There is no other spread. Should this patient be subjected to deep x-ray therapy or to an ovariectomy or hormonal therapy as a precautionary measure?*

M.D., Massachusetts.

Answer.—There is a great difference of opinion in regard to this query. The consensus would be that this patient should have x-ray therapy to the supraclavicular and internal mammary areas on the side of the lesion and should not have an ovariectomy or hormonal therapy until positive indication arises.

ENDOCRINE THERAPY AFTER REMOVAL OF MALIGNANCY

To the Editor:—*A woman, aged 46 years, had a radical mastectomy for a malignancy of the breast about two years ago but no irradiation. The lymph nodes dissected from the axilla were normal, and there have been no signs of regrowth or metastasis to date. Would there be any contraindications to using testosterone for relief of severe menopausal symptoms?* *Leo. J. Greenberg, M.D., Chicago.*

Answer.—At the age of 46, this patient probably has ovarian failure from organic senescence, with lowered estrogen activity and perhaps some elevation of 17-ketosteroids. She has "severe menopausal symptoms," which probably means "flushes" and vasomotor instability. There is still discussion as to the effectiveness of sex hormone therapy in the relief of such symptoms. There apparently are no metastases and no evidence that the tumor was "estrogen dependent." As is known, there is no direct evidence that estrogens are carcinogenic agents in the human. However, most physicians would be unhappy with the addition of any sex steroid in a patient who has no evidence of recurrence or metastasis of breast cancer two years after operation. Psychotherapy, tranquilizing drugs, or barbiturates suggest themselves as preferable alternates to either testosterone or estrogen therapy in relieving what is a temporary inconvenience.

ENURESIS

To the Editor:—*The superintendent of a boys' home has asked me for information concerning a group of bedwetters, aged 14, 15, 16, and even 18 years. These boys have been given ¾ grain (50 mg.) of ephedrine sulfate each night before retiring and have had good results while the drug has been administered; some of them have been cured. Is there any danger in the prolonged use of ephedrine sulfate in these youths as far as cerebral stimulation or other complications are concerned?*

John F. Raycroft, M.D., Brooklyn, N. Y.

Answer.—This consultant cannot sympathize with drug treatment of enuresis as a general procedure, because it is often merely a placebo, and the condition evades diagnosis. Enuresis is most frequently a psychiatric symptom in a multisymptomatic psychiatric disorder. The superintendent of the home should obtain psychiatric service for the youths. Enuresis is a sign of anxiety and psychopathological immaturity of ego development.

GENERALIZED ATOPIC DERMATITIS

To the Editor:—*The answers to the query concerning the management of atopic dermatitis in* The Journal *for March 30, 1957, page 1197, demonstrate the need for more complete understanding of this "strange disease." Atopic dermatitis, or neurodermatitis disseminata (atopic eczema), in all but very young infants does not appear to be a manifestation of specific allergy, with extremely rare exceptions. Elimination diets, cutaneous testing, and desensitization lend little to the management of this disease; in fact, they are generally useless.*

The etiological factors in atopic dermatitis and in duodenal ulcer, ulcerative colitis, migraine, and some cases of asthma and rheumatoid arthritis appear to be similar, if not identical. It is a stress complex, the skin being the organ which reflects the emotional tone of the individual, although other organs or systems may also be affected simultaneously or alternately. Emotional factors dominate as the trigger mechanism in the exacerbations of the disease in those persons who constitutionally react cutaneously to stress. The type of emotional disturbance, of course, varies, although infantile attitudes, repressed aggressions, fears of failure, and guilt complexes seem to be common. Psychiatric management, especially in groups of such individuals, appears to be useful as adjuvant therapy; individual therapy generally has not been as successful.

Hospitalization or drastic curtailment of normal activities is probably not desirable, unless there are specific indications for such, as in the case of marked

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secondary infection or other important complications. Adjustment to the normal stresses of everyday life is a necessity, and the elimination of these stresses for periods of time, although it generally will give relief, does not make for the development of a satisfactory adjustment. Compulsive activity is better controlled by insight than by enforced stoppage; activity is actually a means toward remission.

The use of steroids, locally and/or parenterally, is of considerable aid in the control of exacerbations and for maintenance of severe conditions. If the patient is under careful observation and the smallest doses are used for control, there seems to be little attendant danger of undesirable side-effects in relation to the atopic dermatitis. It is important that dosage be gradually diminished. Rarely, tranquilizers and sedatives have demonstrable desirable effects. Indicated local measures aid in the healing of severely affected areas; antibiotics are useful in the control of secondary infectious processes.

A fuller understanding of this common distressing disease, as well as its relation to other dermatological and systemic diseases, is greatly to be desired. A research foundation for the study of atopic dermatitis should be organized and endowed to this end.

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The above comment was referred to one of the consultants who answered the original query, and his reply follows.—ED.

TO THE EDITOR:—*The comment is a well-considered presentation of the physicians' concept of atopic dermatitis. One must agree that a fuller understanding of atopic dermatitis, as well as the establishment of a special research project or foundation for its study, is to be desired. Such efforts have been made in the past but unfortunately did not meet with success.*

As yet there is great confusion and disagreement about the etiology of atopic dermatitis. Recent articles by Gans (Tr. St. John's Hosp. Dermat. Soc., *no. 37, p. 1, 1956*) *and Baer* (Excerpta Med. *[sec. 13]* **11**:47, *1957*) *well present the conflict of opinion, and so does the recent controversy on the role of allergic factors in atopic dermatitis in the correspondence and editorial sections of the* Journal of Allergy (J. Allergy **27**:293, *480, and 483, 1956*). *The Pennsylvania physicians add their concept to the controversy.*

Atopic dermatitis always has been a mysterious disease which has given rise to much speculation. The French authors who first clearly set apart atopic dermatitis as lichen simplex chronicus (Vidal), neurodermatitis (Brocq), and prurigo diathesique (Besnier) some 70 years ago proposed "autointoxication" and nervous elements as etiological factors. In the 1920's and 1930's allergy became the fashion of the day, to be followed by the concepts of psychosomatic disorders; now it is the stress complex, which according to Selye is the common denominator of disease. Most of these theories have been proposed by men of great knowledge and insight into the problems. Yet there is a tremendous difference of opinion. Obviously a simple hypothesis will not do. One may well accept stress as a mediator of various underlying factors, such as allergic, emotional, infectious, and endocrine, in persons endowed with a peculiar physical and psychological make-up.

There are some statements in the comment of the Pennsylvania physicians which should not go unchallenged, such as the fact that allergic management is generally useless. Allergy plays a great role in some cases of atopic dermatitis at every age, although it is only one factor in the picture; in infantile eczema it is frequently of decisive importance. As the patient grows older, other factors, especially emotional, become more important. Hospitalization in severe cases is of great help so as to give the patient rest and allow a thorough allergic and psychiatric investigation to be made away from the physical and emotional home environment. It is at times the only means which demonstrates to the patient that something can be done for him.

Management of atopic dermatitis is not necessarily dependent on the administration of this or that medicament or the application of this or that theory. It depends much more on the physician, who has an interest in the disease and takes the time to give his patient care and understanding, and on the patient, who is confident that his physician is willing and able to help him.

MONARTICULAR ARTHRITIS AFTER POLIOMYELITIS VACCINATION

TO THE EDITOR:—*Apropos the answer to a query in* THE JOURNAL *for June 29, 1957, page 1035, I should like to call attention to the fact that monarticular arthritis can occur after poliomyelitis vaccination and that this can be evidence of an acute gouty attack. I make this statement because a 35-year-old man, who had never suffered previously from an acute attack of gout, had three such attacks during a seven-month period last year, each within 12 hours after his "polio shot." The response to the administration of colchicine and the clinical picture were typical of gout. I feel certain that other physicians will have a similar experience as more of the poliomyelitis vaccine is used on adults. It is not unusual for other substances, such as liver extract, to precipitate a gouty attack. I should suspect that the high nucleoprotein content of killed viruses might account for such a diathesis.*

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SALTING FRESH MEAT TO REMOVE BLOOD

To the Editor:—*Reference is made to the query concerning the salting of meat and its relation to a salt-free diet, which appears in* The Journal *for July 6, 1957, page 1174. In the correspondence section of* The Journal *for Dec. 19, 1953, page 1472, data provided indicate that meat processed according to Jewish dietary law has its sodium content increased remarkably. However, if the salting is not excessive, cooking takes out practically all the added sodium. Additional comments of interest with respect to salted meat and its treatment by boiling, broiling, frying, or roasting have been made in the correspondence section of* The Journal *for March 27, 1954, page 1114.*

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The above comment was referred to the consultant who answered the original query, and his reply follows.—Ed.

To the Editor:—*It has been almost four years since the publication of the letter in* The Journal *about salt-poor diet and Jewish dietary laws, and some of the information could well bear repeating. Dr. Bruno Kisch has given some data indicating that the processing of raw meat according to Jewish dietary law increases the sodium content remarkably. He found that an average piece of beef containing 55 mg. of sodium per 100 Gm. before being salted contained 234 mg. per 100 Gm. after being salted according to the usual Jewish dietary laws. It was shown that, if salting is not excessive, cooking takes out practically all the added sodium. The soaking of salted meat in cold or warm water before cooking removes the salt sprinkled on the surface quite well, especially if the amount of salt is not excessive. It seems that, if treated meat is to be used in a salt-poor diet, the cook should use a minimum of salt, allow the meat to stand only for the religiously permissible period of time, and cook the meat in a generous amount of fluid and throw away the broth.*

PROLONGED STEROID TREATMENT OF ASTHMA

To the Editor:—*A part of the answer by the first consultant to the query regarding prolonged steroid treatment of asthma in* The Journal *for March 9, 1957, page 908, is, in my experience, wrong. I refer to the sentence wherein the consultant deprecates skin testing for food allergy in children.*

If there is any age group in which food-allergy skin tests closely approach the clinical findings, it is in the case of children. In this group such foods as nuts, fish, eggs, milk, and cereals frequently alert the experienced allergist to one or more of the causes of the allergy, since the younger the patient the greater is the possibility of food allergy being a factor, and its detection is expedited by skin tests expertly utilized.

In this connection the difficulties in the past as well as at the present time stem from certain factors. 1. The technique is poor; a control must be used with each series of tests so as to evaluate hypersensitive reactions, which are really negative but are oftentimes called positive, with consequently incorrect interpretation and clinical result. 2. Skin testing is not a laboratory procedure but requires the personal services of a skilled allergist, both from a safety-to-life standpoint when intracutaneous tests are performed and for the expert evaluation of the findings (correspondence section, J. A. M. A. **152:**355 *[May 23] 1953).*

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PEDIATRIC DOSAGE OF STEROIDS

To the Editor:—*This is with reference to a statement of the consultant in his answer to a query concerning pediatric dosage of steroids which appeared in* The Journal *for July 6, 1957, page 1174.*

The consultant stated: "Prolonged use of cortisone will suppress growth of children when used in doses of 45 mg. or less per square meter of body surface daily." I believe the phrase "or less" should really read "or more," inasmuch as a report on the effects of cortisone therapy on the growth of children (Blodgett and others: New England J. Med. **254:**636, *1956), from which possibly the consultant derived his information, states: "A minimum of 45 mg. per square meter [of body-surface area] per day was required to reduce the growth rate of endocrine-normal children."*

This statement bears out some observations by Hill on this subject (New England J. Med. **253:**821, *1955), pointing to the fact that, in a series of allergic children whom he was treating with cortisone over prolonged periods of time, no evidence of retardation of growth could be found sufficient to warrant withholding cortisone when it was needed.*

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The above comment was referred to the consultant who answered the original query, and his reply follows.—Ed.

To the Editor:—*The physician is correct. The statement should read: "Prolonged use of cortisone may suppress growth of children when used in doses of 45 mg. or more per square meter of body surface daily."*